UNIVERSITY OF ALBERTA

Effects of acute moderate intensity FES-leg cycle, arm crank, and hybrid ergometer exercise on lipid-lipoprotein profile in persons with spinal cord injury

by

Christina Barbara Weiss

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Science

Faculty of Physical Education and Recreation

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Dated: Nov. 13, 1998

DEDICATION

To all the subjects in the study who devoted their time, energy, and support so that I could complete my Master of Science.

ABSTRACT

The study investigated the effects of acute moderate intensity (75%) exercise on low density lipoprotein (LDL) cholesterol, total high density lipoprotein (HDL) cholesterol, HDL_2, HDL_3, triglycerides, and total cholesterol levels. Eight persons with spinal cord injury (SCI)(four: C5-C7 and four: T4-T8), average age 42.5 years (range: 30-53 yrs) and 18 years post-SCI (range: 3-40 yrs) performed eight weeks of functional electrical stimulation-cycle training (FES-T) followed by four consecutive days of FES (FES-A), arm crank ergometer (ACE-A), and Hybrid ergometer (HE-A) training with one week of rest between treatments. Subjects completed three 3-day dietary records (DR) at week 1, 9, 17, and pre- and post- treatment blood testing. Single subject analyses revealed a positive nonsignificant trend in HDL levels after performing HE-A. Results also showed significantly increased caloric ($p=0.05$, $p<0.05$), carbohydrate ($p=0.01$, $p<0.016$), and fat ($p=0.01$; $p<0.016$) consumption between the second and third DR with no significant changes in weight. Computed work rate, power output, and energy expenditure with ACE-A and HE-A were significantly ($p<0.017$) higher than FES-A in all cases. HE-A training is therefore recommended as an optimal way to improve HDL levels, and reduce the risk of cardiovascular disease in persons with SCI.

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TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION 1

Rationale for the study 3

Statement of the problem 4

Purpose of the study 5

Research hypotheses 5

Definitions 6

Limitations 7

Delimitations 8

Exclusion Criteria 8

Inclusion Criteria 8

CHAPTER 2: LITERATURE REVIEW 9

CVD in non-disabled people 9

CVD costs 9

Atherogenic lipid-lipoprotein profile 10

Part 1: Biochemistry of lipid metabolism 10

Introduction 10

Adipose tissue and lipid metabolism 10

Glucose transport within adipose tissue 11

Triacylglycerol mobilization 12

Catecholamines and adrenoreceptors in adipocytes 12

Insulin and anti-lipolysis 15

Lipid oxidation and its effects on glucose 15
Regulation of lipid mobilization during exercise 16
Molecular cell biology of adipose tissue 18
Energy balance and basal metabolic rate (BMR) 18
Regional and gender differences in fat mobilization 18
Lipids and lipoproteins 19
Membrane cholesterol 19
Structure of lipoproteins 19
Lipoprotein lipase (LPL) 22
Kinetics of the LPL reaction 22
Reverse cholesterol transport 23
Lecithin: cholesterol acyltransferase (LCAT) 23
Cholesteryl ester transfer protein (CETP) 23
Hepatic lipase 24
The apo A-I cycle 24
Removal of LDL from the circulation 25
The LDL receptor pathway 26
Atherosclerosis 27
Part 2: CVD in SCI 32
Reduced HDL 33
Etiology of reduced HDL levels in people with SCI 35
The sympathetic nervous system (SNS) 35
Physical inactivity 35

Reduced muscle mass 36
Glucose transporters 37
Lipoprotein lipase (LPL) dysfunction 37
Part 3: Exercise 38
LPL and HL 39
Effects of intensity on LPL activity 40
Weight loss and energy expenditure 40
Functional electrical exercise for persons with SCI 42
Benefits of FES-Assisted Exercise 43
Use of large muscle 43
Increased cardiac muscle 47
Improved circulation &
increased cardiopulmonary fitness 47
Enhanced rehabilitation 48
Increased catecholamine levels in people with SCI 48
Lipid and glucose mobilization in SNS versus
catecholamines 51
Benefits of hybrid exercise 52
FES-LCE or HE exercise 54
Part 4: Methodology 55
Dietary intake estimation 55
Dietary history 55
24-hour recall 55

Food frequency questionnaires 56
Multiple day dietary food record 57
Combining dietary resources 58
CHAPTER 3: METHODS & PROCEDURES 60
Recruitment 60
Subjects 60
Study overview 61
Procedures 62
Methods 63
Three-day dietary food record 63
Blood sampling procedure 64
Lipid analysis 64
Blood sample storage 65
Maximal aerobic power determination 66
Criteria for maximal aerobic power (VO_2 max) 67
Maximal FES-leg cycle ergometer (FES-LCE) test 67
Maximal arm crank ergometer (ACE) test 68
Maximal hybrid ergometer (HE) test 68
FES-training (FES-T) 69
FES-acute (FES-A) 70
ACE-acute (ACE-A) 70
Hybrid-acute (HE-A) 71
Blood pressure 71

Heart rate 71
Weight 71
Energy expenditure 72
Power output 72
Data collection 72
Data analysis 73
Ethical considerations 74
Safety 75
Autonomic dysreflexia 75
Thermoregulatory dysfunction 76
Bruising 76
Electrode burning 76
CHAPTER 4: RESULTS 78
Lipids group analysis 78
Difference between Quads and Paras 81
Dietary analysis 90
Single subject analysis (lipids, dietary analysis, and summary) 91
Subject #1 91
Subject #2 95
Subject #3 99
Subject #4 103
Subject #5 107
Subject #6 111

Subject #7 115
Subject #8 119
Exercise testing 123
Difference between Quads and Paras 124
Exercise training 124
Resistance 125
Work rate 126
Difference between Quads and Paras 126
Power output 127
Difference between Quads and Paras 127
Energy expenditure 128
Difference between Quads and Paras 128
Correlations 129
CHAPTER 5: DISCUSSION 148
Subjects 148
Lipid levels: group analysis 148
Lipid levels with training 151
Group analysis with percent change 152
Difference between quads and paras 158
Single subject analysis 158
Dietary analysis 161
Exercise testing 162
Procedures 162

Heart rate 163
Borg-RPE scale 163
VO_2max 164
Resistance 165
Power output 165
Exercise training 166
Time completed 166
Work rate 167
Power output 167
Intensity 168
Caloric expenditure 168
Correlations 169
CHAPTER 6: SUMMARY AND CONCLUSION 171
Future directions 176
Conclusion 177
REFERENCES 179
APPENDICES 203
Appendix A: Adult Treatment Panel II 204
Appendix B: Study Information for the Participant 209
Appendix C: Form of Consent 213
Appendix D: Study Overview 215
Appendix E: 3-Day Dietary Intake Record 217
Appendix F: Borg-Rate of Perceived Exertion (RPE) Scale 220

LIST OF FIGURES

2.1. Activation of lipolysis via adrenoreceptor-coupled mechanisms 14

2.2. Metabolic scheme 17

2.3. Major cholesterol transport pathways between liver and peripheral tissues 21

2.4. Schematic diagram of reverse cholesterol transport 25

2.5. The intimal traffic of cholesterol: schematic representation of processes leading to the formation of foam cells and extracellular cholesterol core 30

2.6. Overview of some potentially important factors involved in the adaptation of lipid transport and plasma lipoprotein levels to endurance-exercise training 45

2.7. Overview of the autonomic nervous system, sympathetic and parasympathetic divisions, issuing from the brain and the spinal cord 49

4.1. Percent change in HDL, HDL_2, HDL_3, TC/HDL, HDL_2/HDL_3 for group (n=8) with FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 80

4.2. Percent change in LDL, TG, and TC for group (n=8) after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 81

4.3. Percent change in HDL levels in people with quadriplegia (Quads) versus people with paraplegia (Paras) after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 82

4.4 Percent change in HDL_2 levels in Quads (n=4) versus Paras (n=4) after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 83

4.5 Percent change in HDL_3 levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 84

4.6. Percent change in TC/HDL ratio in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 85

4.7. Percent change in HDL_2/HDL_3 ratio in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 86

4.8. Percent change in LDL levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels. 87

4.9. Percent change in TG levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 88

4.10. Percent change in TC levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels. 89

4.11 Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#1) with quadriplegia after performing FES-A, FES-A, ACE-A, and HE-A relative to baseline levels 91

4.12. Percent change in LDL, TG, and TC in a subject (#1) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 93

4.13. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#2) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 95

4.14. Percent change in LDL, TG, and TC in a subject (#2) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels. 97

4.15. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#3) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 99

4.16. Percent change in LDL, TG, and TC in a subject (#3) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 101

4.17. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#4) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 103

4.18. Percent change in LDL, TG, and TC in a subject (#4) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 105

4.19. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#5) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 107

4.20. Percent change in LDL, TG, and TC in a subject (#5) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 109

4.21. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#6) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 111

4.22. Percent change in LDL, TG, and TC in a subject (#6) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels. 113

4.23. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#7) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 115

4.24. Percent change in LDL, TG, and TC in a subject with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels. 117

4.25. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#8) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 119

4.26. Percent change in LDL, TG, and TC in a subject (#8) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels 121

5.1. Summary of the effects of prolonged endurance-exercise in initially sedentary, overweight individuals 156

A. Flow chart of primary prevention in adults without evidence of coronary heart disease (CHD) 206

B. Flow chart of secondary prevention in adults with evidence of coronary heart disease (CHD) 207

C. Flow chart of primary prevention in adults without evidence of coronary heart disease (CHD) 208

LIST OF TABLES

3.1 Subject characteristics 61

4.1 Means and standard deviations for all lipid variables 78

4.2 Means and standard deviations of lipid and lipoprotein ratios 79

4.3 Means and standard deviations of all diet variables 89

4.4 Maximal heart rate (bts/min), Borg-RPE scale and peak VO_2 (L/min) during maximal testing 123

4.5 Resistances for FES-T, FES-A, ACE-A, and HE-A 125

4.6 Work rate (W) 126

4.7 Training power outputs (W) for FES-T, FES-A, ACE-A, and HE-A 127

4.8 Subject caloric expenditures (Kcal) during an average workout at 75% exercise intensity 128

4.9 HDL levels over time (mmol/L) 130

4.10 HDL levels relative to rest expressed as percent change (%) 131

4.11 HDL levels relative to baseline expressed as percent change (%) 131

4.12 HDL_2 levels over time (mmol/L) 132

4.13 HDL_2 levels relative to rest expressed as percent change (%) 133

4.14 HDL_2 levels relative to baseline expressed as percent change (%) 133

4.15 HDL_3 levels over time (mmol/L) 134

4.16 HDL_3 levels relative to rest expressed as percent change (%) 135

4.17 HDL_3 levels relative to baseline expressed as percent change (%) 135

4.18 TC/HDL ratio over time (mmol/L) 136

4.19 TC/HDL ratio relative to rest expressed as percent change (%) 137

4.20 TC/HDL ratio relative to baseline expressed as percent change (%) 137

4.21 HDL_2/HDL_3 ratio over time (mmol/L) 138

4.22 HDL_2/HDL_3 ratio relative to rest expressed as percent change (%) 139

4.23 HDL_2/HDL_3 ratio relative to baseline expressed as percent change (%) ... 139

4.24 LDL levels over time (mmol/L) 140

4.25 LDL levels relative to rest expressed as percent change (%) 141

4.26 LDL levels relative to baseline expressed as percent change (%) 141

4.27 TG levels over time (mmol/L) 142

4.28 TG levels relative to rest expressed as percent change (%) 143

4.29 TG levels relative to baseline expressed as percent change (%) 143

4.30 TC levels over time (mmol/L) 144

4.31 TC levels relative to rest expressed as percent change (%) 145

4.32 TC levels relative to baseline expressed as percent change (%) 145

4.33 Dietary variables in first, second, and third dietary record 146

4.34 Weight and calories/weight ratio over time 147

5.1 Calculated sample size at power = 0.80, $\alpha = 0.05$, and df = 4 for lipid and lipoprotein variables 152

LIST OF ABBREVIATIONS

ACE:	Arm Crank Ergometer
ACE-A:	Arm Crank Ergometer Training
apo:	Apo(lipo)protein
Borg-RPE:	Borg-Rate of Perceived Exertion Scale
BP:	Blood Pressure
cAMP:	Cyclic Adenosine Monophosphate
cATP:	Cyclic Adenosine Triphosphate
CETP:	Cholesteryl Ester Transfer Protein
CVD:	Cardiovascular Disease
FES:	Functional Electrical Stimulation
FES-A:	Functional Electrical Stimulation Acute Training
FES-LCE:	Functional Electrical Stimulation Leg Cycle Ergometer
FES-T:	Functional Electrical Stimulation Training (Eight Weeks)
FFA:	Free Fatty Acids
HDL:	High Density Lipoprotein
HDL_2,HDL_3:	High Density Lipoprotein Subfractions
HE:	Hybrid Ergometer
HE-A:	Hybrid Ergometer Acute Training
HL:	Hepatic Lipase
HMG-CoA:	3-Hydroxy-3 methylglutaryl-Coenzyme A
HR:	Heart Rate

HRmax:	Maximal Heart Rate
ibid:	Ibidem
IDL:	Intermediate Density Lipoprotein
LCAT:	Lecithin: Cholesterol Acyltransferase
LDL:	Low Density Lipoprotein
LLP:	Lipid-Lipoprotein Profile
ox-LDL:	Oxidized Low Density Lipoprotein
Paras:	People With Paraplegia
Quads:	People With Quadriplegia
RCT:	Reverse Cholesterol Transport
RER:	Respiratory Exchange Ratio
SCI:	Spinal Cord Injury
SNS:	Sympathetic Nervous System
TG:	Triacylglycerol
V_E:	Pulmonary Ventilation
VLDL:	Very Low Density Lipoprotein
VO_2:	Oxygen Consumption
VO_2 max:	Maximal Aerobic Power

CHAPTER 1
INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death, disability, and illness among Canadians with or without a disability (Nair, Nargundkar, Johansen, & Strachan, 1990). Disease of the heart and blood vessels include a broad group of conditions (Berne & Levy, 1992). When these conditions develop, blood flow through the circulatory system is compromised. Different types of CVD include atherosclerosis (blockage of arteries, particularly the coronary arteries); arrhythmias (disturbance of heart rhythm); hypertension (high blood pressure); valvular heart disease (conditions of the heart valves); peripheral vascular disease (atherosclerosis affecting large peripheral arteries), and myocardial disease (conditions affecting the heart muscle) (Heart and Stroke Foundation (HSFC), 1993). The two leading types of CVD are ischemic heart disease and stroke, due to reduced blood flow to the heart and brain, respectively (HSFC, 1993).

Atherosclerosis is the principal cause of heart attack, stroke, and gangrene of the extremities. Atherosclerosis begins as a protective response to insults or injury to the endothelium and smooth muscle cells of the wall of the artery. The process consists of the formation of fibrofatty and fibrous lesions, preceded and accompanied by inflammation. These lesions, when excessive, may occlude arteries (Ross, 1993).

Research into the causes of CVD has identified more than 200 risk factors which have traditionally been divided into two categories: modifiable and nonmodifiable (Castelli, 1996). The modifiable risk factors are cigarette smoking, high blood pressure, high blood cholesterol level, reduced high density lipoprotein cholesterol (HDL) level, diabetes, obesity, and physical inactivity (Castelli, 1996; Genest & Cohn, 1995; MacLean, 1994b; Nair et al.,1990; Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: National cholesterol education program (NCEP), 1988). Among these, the most important are 1) abnormal lipids, some of which are very atherogenic, 2) high blood pressure, 3) cigarette smoking, and 4) physical inactivity (Arrol & Swinburn, 1994; Castelli, 1996). Nonmodifiable risk factors are age, gender, and hereditary factors (Genest & Cohn, 1995).

Reduced levels of HDL particles, the "good cholesterol," are a risk factor for CVD. HDL is felt to be protective by removing excess cholesterol from cells such as those in the artery wall (Henry, 1991). A reduced level of HDL could therefore result in accumulation of excess cholesterol in these cells. High levels of low-density lipoprotein cholesterol (LDL), the "bad cholesterol," and triacylglycerols (TG), on the other hand, are harmful (Henry, 1991). High levels in the human body have been directly correlated with an increased risk of coronary heart disease and are often found in atherosclerotic plaque deposits (Campbell, 1995). Thus, any intervention that would ultimately increase HDL levels and decrease LDL and TG would potentially decrease the risk of coronary artery disease.

People with spinal cord injury (SCI) have reduced levels of HDL notably due to decreased physical activity (Dallmeijer, Hopman, Lucas, & van der Woude, 1997). Physical activity has demonstrated its ability to increase HDL in people with or without a disability (Berg, Frey, Baumstark, Halle, & Keul, 1994). Furthermore, people who perform exercise show profound increases in HDL compared to sedentary people (Wood, Williams, & Haskell, 1984; Dallmeijer et al., 1997). However, longitudinal studies which have investigated HDL levels do not consistently find significant increases with exercise (Wood et al. 1984). Moreover, how much and which type of exercise remains controversial. In fact, a meta-analysis of studies demonstrated that an average exercising subject usually decreased HDL by only 0.03 mmol/L (p=not significant), whereas total cholesterol decreased 0.26 mmol/L, TG decreased 0.18 mmol/L, and LDL decreased 0.13 mmol/L (Vu Tran, Weltman, Glass, & Mood, 1983).

Recently, research has revealed that although a single bout of exercise can induce short term transient increases in HDL (Pronk, 1993, Hubinger & Mackinnon, 1992), HDL do not usually increase until an average training level of 10 miles/week or more (>1,000kcal/week) is achieved during a period of four weeks to one year (Després & Lamarche, 1994;Williams, Wood, Haskell, & Vranizan, 1982; Wood et al., 1984). Literature also suggested that training for 5-10% increases in HDL should be performed at a moderate intensity of 50-75% of maximum heart rate or 60-79% maximum oxygen consumption, at least three times a week where each session should expend more than

300 kcal per session (American College of Sports Medicine (ACSM), 1990; Berg et al., 1994; Crouse et al., 1997; Gordon et al., 1994; Stein et al., 1990; Zmuda et al., 1998).

Due to the potential of exercise to increase HDL levels in people with SCI, there is a need to develop and implement physical exercise programs for people with SCI. To date, functional electrical stimulation (FES), which uses electrical current to contract paralyzed muscles, has offered many new opportunities for people with SCI to participate in exercise. FES-assisted exercises include FES-walking, FES-leg cycling ergometer (FES-LCE), FES-rowing ergometer, and Hybrid ergometer (HE). Hybrid, which incorporates the conventional arm crank ergometer (ACE) with the FES-LCE, has recently been introduced as perhaps the preferred mode of exercise as it elicits superior outcomes in venous return, cardiac volume load, and training oxygen consumption compared to the FES-LCE exercise (Krauss et al., 1993).

At this time, little information is available on the effects of FES-exercise on lipid and lipoprotein profiles in people with SCI. One study has shown that FES-exercise increased HDL (1.13 vs. 1.19 mmol/L) and HDL subfraction three (HDL_3)(0.72 vs. 0.81 mmol/L, $p < .01$), whereas HDL subfraction two (HDL_2) declined (0.40 vs. 0.38 mmol/L) following 4-5 months of training (Brenes, McDermott, & Sikora, 1989). HDL_3 was the only particle that changed significantly. This would suggest a possible decreased risk of coronary heart disease in people with SCI using this form of exercise (Brenes et al., 1989). However promising, research in the long-term prevention of CVD in people with SCI is limited.

Rationale for the Study

Because a higher incidence and risk of CVD is evident in the chronic phase of SCI (Cowell, Squires, & Raven, 1986; DeVivo, Black, & Stover, 1993; Ragnarsson, Pollack, & Twist, 1991) due to factors including reduced HDL levels (Bauman et al.,1992b; Ragnarsson et al., 1991), sedentary lifestyle, (Ragnarsson et al. 1991), and decreased muscle mass (Cowell et al., 1986), it seemed crucial to investigate whether physical activity could reduce risk for CVD and increase HDL levels in people with SCI.

People with SCI have traditionally used ACE, wheeling, and wheelchair sport for

physical activity. These types of exercise can maintain fitness and health in people with SCI, but may also lead to musculoskeletal injuries (Ragnarsson et al., 1991). As the structures of the upper extremity were designed for prehensile activities and are needed for mobility in people with SCI, a) the upper extremities are subject to more frequent and more demanding use which may lead to overuse and pain, and b) the consequences of pain to functional independence are more severe (Waters, Sie, & Adkins, 1993). Therefore, even a 'minor' shoulder problem can cause a marked decrease in functional independence (Waters et al., 1993). In contrast, exercise with FES offers fitness and health benefits without the danger of injuring the upper body as it uses the large paralyzed muscles of the lower extremity (Ragnarsson et al., 1991).

FES-assisted exercise research has discovered many benefits which include increased blood (venous) return (Figoni et al., 1991; Glaser, 1994), improved circulation (Krauss et al., 1993), decreased venous pooling in the extremities (Krauss et al., 1993), increased muscle mass (Sloan, Bremner, Byrne, Day, & Scull, 1994), increased Type IIa oxidative fibres (Andersen et al., 1996), and increased catecholamine response to exercise (Bloomfield, Jackson, & Mysiw, 1994).

Literature suggests that HE exercise has additional benefits to FES-exercise modalities in that it uses a greater muscle mass (Glaser, 1994; Hooker et al., 1992), creates a higher cardiac volume load to promote central cardiovascular training benefits (Figoni et al., 1990; Glaser, 1994; Hooker et al., 1992), enables training at a higher oxygen consumption (Figoni et al., 1990; Glaser, 1994; Hooker et al., 1992; Krauss et al., 1993), and provides training benefits to both upper- and lower-body musculature (Glaser, 1994; Hooker et al., 1992).

Statement of the Problem

Although the FES-LCE and HE have reported numerous physiological benefits, there has been limited research on the effects of this exercise on HDL, LDL, and TG, all of which are associated with CVD. Also, there is limited documentation on the level of intensity, duration, and caloric expenditure needed to elicit changes in this profile (Stein, et al., 1990).

Purpose of the Study

This study: 1) determined the effects of ACE, FES-LCE and HE exercise on the lipid-lipoprotein profile, 2) compared FES-LCE and HE exercise to the conventional ACE, 3) investigated the effects of intensity, duration, and energy expenditure on lipid-lipoprotein profile, 4) monitored weight loss and diet as they are associated with HDL, and 5) compared findings of people with quadriplegia to those with paraplegia. Findings from this study were compared to those stated in the literature.

Research Hypotheses

The following twelve hypotheses were investigated.

1. Exercise training at 75% exercise intensity with ACE acute training (ACE-A) and HE acute training (HE-A) would improve HDL, HDL_2, and HDL_3 and would reduce TG, and TC. However, superior increases would occur with HE-A.
2. Exercise training with FES training (FES-T) and FES acute training (FES-A) would not elicit changes in HDL, HDL_2, or HDL_3, however TG and TC would be reduced.
3. No changes would be found in LDL after performing FES-T, FES-A, ACE-A or HE-A.
4. There would be no differences in the lipid-lipoprotein profile with training in people with quadriplegia or paraplegia relative to baseline.
5. There would be no differences in the lipid-lipoprotein profile between people with quadriplegia and those with paraplegia at baseline and with exercise.
6. Trends in lipid-lipoprotein profile would be evident in subjects after single subject analyses.
7. Weight loss would occur to a greater extent with HE-A than with ACE-A, FES-T or FES-A.
8. HE-A would elicit superior increases in resistance, power output and energy expenditure than FES-A, and ACE-A. ACE-A would elicit superior increases in resistance, power output and energy expenditure than FES-A.

9. Heart rate during maximal testing would be highest with ACE, moderately high with HE, and lowest with FES-LCE.
10. Borg-RPE Scale scores would be similar between ACE and HE and lowest with FES-LCE.
11. Maximal aerobic power would be highest with HE, moderately high with ACE exercise and lowest with FES-LCE.
12. People with paraplegia would have higher heart rates, Borg-RPE Scale recordings and maximal aerobic power measurements.

The above hypotheses were tested in a prospective, non-randomized study involving eight subjects. Subjects were required to complete eight weeks of FES-T, followed by four consecutive days of FES-A, ACE-A, and HE-A. Each intervention was separated by one week of rest. Each subject was assessed in terms of blood lipids and lipoproteins, diet, weight, and training resistance, power output, and energy expenditure.

The results of this study provided information about lipid-lipoprotein profiles and dietary behaviours of people with SCI. In addition, the results provided insight on different modes of exercise and their potential for reducing CVD risk.

Results were beneficial to the subjects in the study in terms of providing information about their health and perhaps to other working people who lead a sedentary lifestyle. Furthermore, this study educated professionals who work with people with SCI about exercising opportunities and their potential for reducing CVD risk factors.

Definitions

Arm Crank Ergometry (ACE): Exercise apparatus used to train the upper body musculature. It requires that the arms crank pedals of a modified mounted bicycle.

Functional Electrical Stimulation (FES): The computerized application of electrical current to paralyzed muscle. This procedure enhances the rebuilding of paralyzed muscles and provides neuromuscular reeducation (Claudine, 1993, p.559).

FES-Leg Cycle Ergometer (FES-LCE): A computerized bicycle which uses FES to stimulate paralyzed muscles (quadriceps, hamstrings, gluteal) sequentially in order to

propel pedals in a cycling motion.

Hybrid Ergometry (HE) Exercise: A type of exercise that involves both the use of the upper and lower body limbs. It is the combination of FES-LCE and ACE. The ACE is placed on a table over the legs, so that both can be performed simultaneously.

Risk factor: Aspects of personal behaviour, lifestyle, environmental exposure, or inherited characteristics, which on the basis of epidemiologic evidence, are known to be associated with CVD.

Autonomic Dysreflexia: A syndrome of reflex sympathetic discharge unique to SCI individuals with lesions above T6 (Ashley et al., 1993). Autonomic dysreflexia is characterized by hypertension, piloerection (sympathetic), headaches, and bradycardia (parasympathetic) and is usually triggered by a nociceptive stimulus causing an exaggerated catecholamine response (Burnham et al., 1994) (see Chapter 3-safety).

Limitations

1. The SCI population in Edmonton is relatively small. This, unfortunately, affected the number of subjects recruited.
2. Individuals with SCI are often approached to participate in other research studies, which decreased the recruitment pool for the study.
3. As some people with SCI required public transport, the time and money needed discouraged people to participate in the study.
4. Due to the invasiveness of the study, some people refrained from participating.
5. Depending on level of lesion, some individuals were intolerant to the electrical stimulus (autonomic dysreflexia) and were denied participation in the study.
6. Some subjects were burnt by surface electrodes and had to take time off from FES training in order to recover.
7. Since dietary records were completed at baseline, after eight weeks of FES-T, and after R4, it was difficult to determine when subjects may have changed dietary behaviours.

Delimitations

This study was limited to eight persons with SCI, seven males and one female, between the ages of 30 and 53 and three to forty years post-SCI. The self-selected subject sample was from the SCI population in Edmonton, Alberta, Canada. The failure to sample randomly from the population affected the strength of any conclusions about the effects caused by the training interventions and implied that the researcher was not justified in extending results beyond the bounds of the experiment itself (Keppel, 1973).

The training modalities were restricted to aerobic non-weight bearing activity (FES-T, FES-A, ACE-A, and HE-A). Physiological variables were delimited to maximal aerobic power, maximal heart rate, blood pressure, energy expenditure, power output, and work rate. Lipid variables were delimited to HDL, HDL_2, HDL_3, LDL, TG, TC, TC/HDL, HDL_2/HDL_3. Dietary intake records were restricted to three days including two week days and one weekend day. Diet variables were delimited to calories, protein, carbohydrates, fat, percent fat, grams of fat, and calorie/weight ratio.

Exclusion criteria

Individuals with pacemakers, uncontrolled arrhythmia, congestive heart failure, current deep venous thrombosis or pulmonary emboli, severe autonomic dysreflexic response to electrical stimulation, severe skin reaction to surface electrodes or electrical stimulation, range of motion less than 90 degrees of flexion at the hips and knees, or severe lower extremity spasticity were excluded from the study.

Individuals who participated in regular planned activity (more than two times a week) were also excluded from the study.

Inclusion criteria

Individuals who passed medical screening were eligible for the study. Subjects with an upper motor neuron lesion, impaired sensation, minimal to moderate spasticity, functional lower extremity joint range of motion, and between a non-dysreflexic and moderate autonomic dysreflexic response to FES (blood pressure < 200/115 mmHg or less than a 50% rise in blood pressure from resting levels) were included in the study.

CHAPTER 2
LITERATURE REVIEW

CVD in Non-Disabled People

CVD principally due to ischemic heart disease and stroke is the leading cause of death and disability in Canada (Horlick, 1994; MacLean, 1994a, 1994b; Nair et al., 1990; Wilkens, 1995). CVD accounts for the largest number of patient days in the hospital among men and women (Randhawa & Riley, 1995). It accounted for 18.6% of deaths in 1921, 46.6% of deaths in 1981, 43% of deaths in 1988 (Nair et al., 1990) and 39% of deaths in 1990 (HSFC, 1993; MacLean, 1994b). Trends show that: a) males consistently have a higher rate of death from CVD than females for all regions of Canada (Nair et al., 1990); b) there are significant differences in the ratios of disease and disability for those individuals of different socioeconomic classes, with those in the lower categories at a much greater disadvantage (MacLean, 1994a); and c) death rates are about four times higher for those 75 years of age and older when compared to individuals less than 65 (Nair et al., 1990).

CVD Costs

CVD costs the Canadian Health Care System an estimated $17 billion annually; five billion dollars are attributed to direct costs, and twelve billion are attributed to indirect costs (MacLean, 1994b; HSFC, 1993). Direct costs refer to the value of resources actually expended and indirect costs are those equalling the value of lost productivity due to illness or disability, and the loss of future earnings by people who die prematurely (HSFC, 1993). Costs associated with CVD are greatest for persons with multiple risk factors (Schauffler, D'Agostino, & Kannel, 1993) such as: age (man over age 45 years; woman over age 55 years or with premature menopause without estrogen replacement therapy); family history of premature CVD; smoking; hypertension; HDL of <0.90 mmol/L; and diabetes (NCEP, 1994).

Atherogenic lipid-lipoprotein profile

Alterations in risk due to lipid and lipoproteins are noted with: (a) total cholesterol (TC) greater than 4.63 mmol/L (Horlick, 1994; Kokkinos et al.,1991); (b) LDL greater than 3.4 mmol/L; (c) HDL less than 0.9 mmol/L and, (d)TC/HDL ratio greater than 5.0 (Kokkinos et al., 1991). The risk for CVD increases in the presence of two or more of these abnormalities. Conservative indications for therapy in men and women are: TC levels greater than 5.79 mmol/L and 6.17 mmol/L respectively, and LDL levels greater than 3.86 mmol/L and 4.1 mmol/L, respectively (Kannel, 1995). Any TC/HDL ratio greater or equal to 5.0 for women and greater or equal to 5.5 for men warrants treatment. Treatment usually begins with dietary intervention and proceeds with drug treatment (NCEP, 1994)(See Appendix A).

As lipids and lipoproteins are the focus of this research, a review (part one: Biochemistry of lipid Metabolism) has been provided. This review will also describe theories of the etiology and pathology of atherosclerosis. With this understanding, the etiology of cardiovascular disease in people with SCI (part two: CVD in SCI) will be discussed followed by mechanisms for prevention through exercise (part three: Exercise). Proceeding this review of literature will be a section (part four: Methodology) on the methodology used in the study.

Part 1: Biochemistry of Lipid Metabolism

Introduction.

Caloric consumption (in the form of fat and carbohydrate) during times of decreased energy requirement is stored in tissues, notably adipose tissue, to be used at a later time. Excess dietary fat and calories are associated with disease states such as diabetes and CVD.

Adipose Tissue and Lipid Metabolism.

Originally considered as simply a storage organ for triacylglycerol (TG), interest in the biology of adipose tissue has increased substantially within the last decade

(Bernlohr & Simpson, 1996). Research has demonstrated that the adipocyte is not a passive lipid storage depot but a cell type that plays a fundamental role in vertebrate energy balance and overall body homeostasis. The primary function of adipose tissue is to serve as a storage site for excess energy (free fatty acids (FFA), glucose) derived from food consumption. Most ingested lipid is found as TG. Fat molecules are initially acted upon by esterases and lipases in saliva and gastric secretions. The lipid mixture is emulsified by the churning motion of the stomach into coarse particles that pass through to the intestine. Lipases in the intestine facilitate the absorption or transport of long chain fatty acids and fatty acyl glycerols. These are reesterified by the intestinal cells and packaged into lipoprotein particles termed chylomicrons that are shuttled into the blood stream via the lymphatic system. At the adipose tissue beds, fatty acids are liberated from circulating TG by lipoprotein lipase (Bernlohr & Simpson, 1996).

Glucose transport within adipose tissue.

To ensure a ready supply of glycolytic intermediates for TG synthesis, fat cells also express specific glucose transporters (Bernlohr & Simpson, 1996). There are two primary types of glucose transport proteins in adipose tissue: GLUT1 and GLUT4. These are also found in skeletal muscle and cardiac tissue (Block, Menick, Robinson, & Buse, 1991). GLUT1 has been shown to be distributed among tissues and present in the plasma membrane of cells unstimulated by insulin, facilitating glucose transport down a concentration gradient (Bernlohr & Simpson, 1996; Block et al., 1991). GLUT4 is almost exclusively found in small, intracellular vesicles in unstimulated adipocytes, but rapidly translocates to the plasma membrane following insulin stimulation (Bernlohr & Simpson, 1996; Block et al., 1991). Insulin promotes GLUT4 recycling and trafficking which results in a net ten to fifteen fold stimulation of hexose transport in response to insulin (Bernlohr & Simpson, 1996). Glucose 6-phosphate can only proceed to the glycolytic pathway because adipocytes do not express significant levels of glucose 6-phosphatase (ibid.). Adipocytes readily convert the products of glycolysis (pyruvate) into fatty acids, which are subsequently esterified with CoA, condensed with alpha-glycerol phosphate to generate TG (ibid.).

Triacylglycerol mobilization.

During times of stress such as fasting or prolonged strenuous exercise the adipocyte's TG droplet is degraded to liberate three FFA and a glycerol moiety (Bernlohr & Simpson, 1996). In these situations, muscle TG is also degraded (Felber, Acheson, & Tappy, 1993). Complete hydrolysis of TG, a process called lipolysis, involves the breakage of three ester bonds by enzymes called lipases. As adipocytes are not able to reuse glycerol, glycerol has no alternative but to be shuttled back to the liver for use in oxidation or gluconeogenesis. Muscle, in contrast, can oxidize glycerol to carbon dioxide or release it into the bloodstream for oxidation in distant tissues. The FFA are immediately bound to serum albumin and carried in the blood stream to the liver, muscle, and other tissues for energy (Felber et al., 1993).

The processes of TG synthesis and hydrolysis are carefully regulated (Bernlohr & Simpson, 1996). Hormone-sensitive lipase, responsible for initiating fatty acid mobilization, is activated by phosphorylation in response to several factors (ibid.).

Catecholamines and adrenoreceptors in adipocytes. The catecholamines epinephrine (EP) and norepinephrine (NE) generated in the inner medullar region of the adrenal glands are perhaps the strongest physiological lipolytic stimuli (Bernlohr & Simpson, 1996). Under basal conditions, the plasma content of NE is three to four times greater than that of EP (Turgan et al., 1996). Stimulation of the adrenal gland by the sympathetic nervous system (SNS) leads to the secretion of catecholamines into the bloodstream (Bernlohr & Simpson, 1996; Turgan et al., 1996). In addition, adipose tissue is itself directly innervated by the SNS to release its neurotransmitter, NE, from terminal nerve endings directly into adipose, where its effects on the adipocyte are mediated by specific plasma membrane adrenoreceptors (Bernlohr & Simpson, 1996; Turgan et al., 1996).

Adipocytes express a combination of five different adrenoreceptor isoforms: α_1, α_2, β_1, β_2, β_3. Lipolysis is signalled by β-adrenergics, and anti-lipolysis is signalled by the α_2-adrenergics (see Figure 2.1.)(Arner, 1995; Bernlohr & Simpson, 1996). In short, although lipolysis is the observed outcome of catecholamine stimulation, it is simply the

steady state result of competition between two opposing pathways triggered by the same signal (Bernlohr & Simpson, 1996; Guyton, 1986).

The mechanisms of signal transduction begins with the binding of catecholamines, or other lipolytic hormones such as adrenocorticotropic hormone and glucagon, to the β-adrenoreceptors which activates adenylyl cyclase via a stimulatory G-protein (Arner, 1995; Belfrage, Fredrikson, Strålfors & Tornqvist, 1984; Bernlohr & Simpson, 1996). Adenylyl cyclase catalyzes the conversion of adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP) (Arner, 1995; Bernlohr & Simpson, 1996). cAMP binds the regulatory subunit of protein kinase A, releasing the active catalytic subunit. Active protein kinase A in turn phosphorylates the hormone-sensitive lipase, which translocates to the TG droplet and begins to hydrolyze the stored lipid. The same signal bound to α_2-adrenoreceptor affects an inhibitory G-protein (Gi), which inhibits the activity of adenylyl cyclase. Disappearance of cAMP eventually causes cAMP to dissociate from the regulatory subunit of protein kinase A, which then inactivates the catalytic subunit by reassociation. In the absence of continued phosphorylation, dephosphorylation inactivates the hormone-sensitive lipase (Bernlohr & Simpson, 1996) (see Figure 2.1).

In contrast to catecholamines, insulin reverses the lipolytic effect and restores the activatability of the enzyme activity. In fact, insulin shifts the steady-state distribution of the phospho- and the dephosphoenzyme to a more dephosphorylated state (Belfrage et al., 1984). This mechanism of insulin involves the inhibition of the phosphorylating reaction, activation of the dephosphorylating reaction, or both (Belfrage et al., 1984).

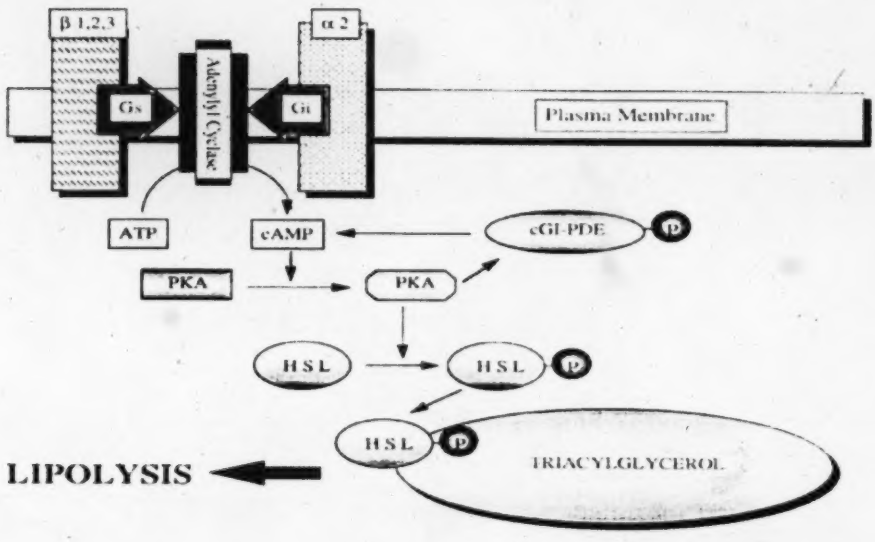


Figure 2.1. Activation of lipolysis via adrenoreceptor-coupled mechanisms. Binding of lipolytic agonists to β-adrenoreceptors (β_1, β_2, and β_3) couples to the G protein which in turn activates adenylyl cyclase thereby producing cAMP. cAMP activation of protein kinase A (PKA) results in phosphorylation and activation of hormone-sensitive lipase (HSL). PKA also phosphorylates and activates the cGMP-inhibited cAMP phosphodiesterase (cGI-PDE), providing a feedback system to lower intracellular cAMP. α_2-adrenoceptor activation results in coupling with Gi and a decrease in adenylyl cyclase activity. Dynamic interplay between β and α_2 adrenoceptor regulates the activity of adenylyl cyclase and, therefore, PKA. Reprinted from "Adipose tissue and lipid metabolism," by D.A. Bernlohr and M.A. Simpson, 1996, in D.E. Vance & J.E. Vance (Eds.), Biochemistry of lipids, lipoproteins, and membranes p. 268. Copyright 1996 with permission from Elsevier Science B.V.

Another pattern of receptor regulation is demonstrated by the use of agonists and antagonists for each receptor isotype (Bernlohr & Simpson, 1996). At very low agonist concentrations, only α_2-receptor activity is observed (i.e., anti-lipolysis). As the agonist concentration is increased, β_1 becomes active and initiates lipolysis. The interplay

between the various isotypes is responsible for the adrenergic balance of lipolysis and anti-lipolysis. In general, α_2-mediated anti-lipolysis modulates resting adipocyte activity, whereas during stress-induced NE release, increased binding to the β-adrenergics overcomes the α_2-inhibitory effect and β-mediated lipolysis prevails (Bernlohr & Simpson, 1996).

Insulin and anti-lipolysis. Insulin, which counteracts the effects of lipolytic stimuli such as catecholamines, is the most important physiological stimulus for energy storage (Bernlohr & Simpson, 1996; Martin, 1996). It is a polypeptide hormone released by pancreatic beta cells in response to elevated blood glucose levels (Bernlohr & Simpson, 1996).

When insulin binds to the adipocyte insulin receptor, lipogenesis is stimulated and lipolysis is inhibited (Bernlohr & Simpson, 1996). Insulin action effectively clears fatty acids and glucose from the blood both by increasing uptake and storage, and by decreasing mobilization of stored energy. Although the mechanism of action is highly complex, insulin inhibits the cAMP cascade (including activation of hormone sensitive lipase) through cleavage of cAMP and direct dephosphorylation of protein kinase A-activated substrates. Dephosphorylation also activates acetyl-coenzyme A (CoA) carboxylase, the enzyme that catalyzes the first committed step in de novo fatty acid synthesis, and fatty acyl-CoA synthetase, the first enzyme in the TG synthetic pathway. Glucose transport is stimulated via GLUT4 translocation to the plasma membrane, and lipoprotein lipase secretion is enhanced (Bernlohr & Simpson, 1996).

The concerted insulin-induced actions of fatty acid/glucose uptake and TG synthesis reduce blood glucose and aid in clearance of fats from the plasma (Bernlohr & Simpson, 1996). Eventually the diminished glucose levels signal the pancreas to stop secreting insulin and initiate secretion of glucagon (ibid.).

Lipid oxidation and its effects on glucose. The effects of FFA on glucose are most clearly represented in obesity where increased fat oxidation inhibits glucose oxidation (Felber et al., 1993). The mechanism postulated for the inhibition of glucose oxidation by

FFA as a result of fat oxidation (from muscle or fat TG) involves an elevation of ratios acetyl-CoA/CoA and $NADH/NAD^+$ and an accumulation of cytosolic citric acid intermediates (predominantly citrate), which act as signals to inhibit the activity of the enzyme complex pyruvate dehydrogenase and phospho-fructokinase (see Figure 2.2).

Regulation of lipid mobilization during exercise. Two factors play a dominant role in the regulation of lipid mobilization from adipose tissue and TG stores within muscle fibres during exercise; blood flow and hormonal changes (Arner, 1995; Martin, 1996). Muscle glycogen breakdown works in a similarly complex mechanism as adipose tissue, where EP binds to phosphorylase a, initiates glycogen breakdown, and increases lactate production which returns to the liver for glucose synthesis (Turgan et al., 1996).

The rate of whole body lipolysis and glycogen utilization are dependent on the action of several hormones, the most potent of which are insulin and catecholamines (Arner, 1995; Guyton, 1986; Martin, 1996). During prolonged exercise, feedback signals from glucosensors stimulate the secretion of lipolytic hormones (catecholamines, glucagon, cortisol, and growth hormone) (Turgan et al., 1996). Stimulated plasma catecholamines and sympathetic neural activity rise exponentially with increasing exercise intensity (especially at work rates above 70% VO_2 max), (Martin, 1996). As levels increase, catecholamines initiate an insulin resistance state by increasing β-adrenoreceptor binding to the G protein which results in lipolysis and an increased supply of FFA (Bernlohr & Simpson, 1996; Karlsson, 1997). FFA produce the insulin resistant state by inhibiting the enzyme complex pyruvate dehydrogenase and phospho-fructokinase, through $NADH^+$ and acetyl-CoA accumulation (Felber et al., 1993).

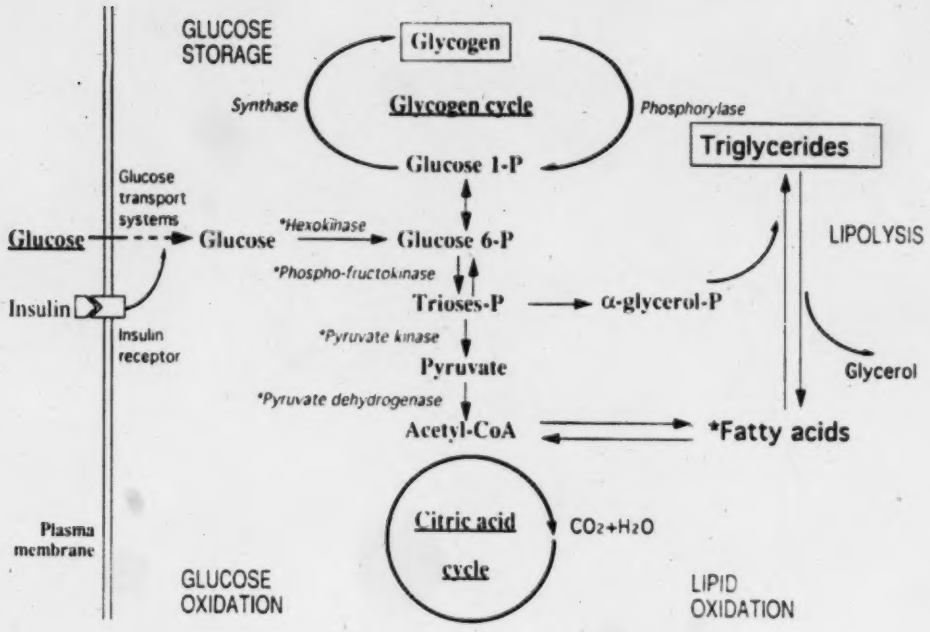


Figure 2.2. Metabolic scheme with the different sites representing insulin receptor binding, the insulin receptor itself, the glucose transport system, the enzymes of the glycogen cycle and the enzymes of the glycolytic pathway, together with the relationship with the fatty acid metabolism. Reprinted from From Obesity to Diabetes, by J.-P. Felber, K.J. Acheson, and L. Tappy (Eds)., Copyright 1993, p.143 with permission from John Wiley & Sons Ltd.

Once FFA accumulate and insulin sensitivity is transiently down-regulated, hepatic glucose production begins, peripheral glucose uptake is inhibited, and peripheral substances (lactate, pyruvate, and alanine) are supplied to the liver (Turgan et al., 1996). In addition, increased sympathetic activity of NE at the sympathetic nerve ending in the Islets of Langerhans diminishes insulin release during exercise (Karlsson, 1997; Martin, 1996; Turgan et al., 1996). The decrease in insulin has a permissive effect that facilitates amplification of the rate of lipolysis in the later stages of prolonged work where plasma catecholamines may attain levels more than 20-fold above those at rest (Martin, 1996).

Molecular Cell Biology of Adipose Tissue.

Energy balance and basal metabolic rate (BMR).

Each organism represents a unique energy equation based upon its feeding habits, exercise patterns, body composition, and environmental conditions (Bernlohr & Simpson, 1996). The net result of the organism's solution to this equation determines its basal metabolic rate (BMR), which is defined in the laboratory as the output of some metabolite per unit of time, measured at rest after an overnight fast (ibid.).

Body size, composition and physical exertion are the most important factors influencing metabolism (Ulijaszek, 1995). Increased body size due to abdominal obesity and muscle mass elevates BMR whereas starvation or semi-starvation, which reduces body fat and muscle, lowers BMR (Bernlohr & Simpson, 1996). Obesity, particularly visceral obesity, tends to increase BMR through grossly increased lipolytic rates due to enlarged adipose tissue and reduced insulin sensitivity. Of note is that the distribution of fat is a relevant factor for BMR, where visceral adipose tissue increases and femoral decreases BMR at rest. Regular strenuous and/or prolonged exercise enhances BMR through increased lean (fat free) body mass which metabolizes primarily fatty acids at rest in the fed state (ibid.). However, the difference between these two states is that adipose tissue, which is insulin resistant, re-circulates FFA in the blood regardless of the demand from tissues, whereas trained muscle tissue either uses FFA for immediate energy or replenishes energy reserves for future exercise bouts.

Regional and gender differences in fat mobilization.

There is good evidence that the lipolytic action of catecholamines is at least 10-fold greater in adipocytes obtained from visceral abdominal adipose tissue than in those from the subcutaneous fat of the extremities (Martin, 1996). Gender and regional differences in the lipolytic response to exercise also exist (Arner, 1995). Females tend to mobilize more lipids from the subcutaneous abdominal area than males, and both sexes have a low rate of lipid mobilization from peripheral subcutaneous areas (Arner, 1995).

Lipids and Lipoproteins.

Membrane cholesterol.

Cholesterol, which is a sterol abundant in mammalian cells, is an essential component of cell membranes (Edwards & Davis, 1996). Cholesterol's most important metabolites are bile acids and steroid hormones. Bile acids serve two important roles: 1) facilitate enzymatic digestion and subsequent absorption of nutrients, especially water soluble fats, and 2) their fecal elimination from the body provides the principal route by which cholesterol homeostasis can be maintained. Thus the amount cholesterol catabolism relative to bile acids appears to be particularly important in the maintenance of whole body cholesterol balance (ibid.).

Structure of lipoproteins.

Plasma lipoproteins are soluble aggregates of lipids and proteins (apo(lipo)proteins) that deliver hydrophobic, water-insoluble lipids [TG and cholesteryl esters (CE)] from the liver and intestine to other tissues in the body for storage or utilization as an energy source (Davis & Vance, 1996). All lipoprotein particles have a common structure of a neutral lipid core (TG and CE) surrounded by a surface monolayer of amphipathic lipids (phospholipids and unesterified cholesterol) and some specific apoproteins (ibid.).

Apoproteins solubilize and stabilize the insoluble lipids of the lipoprotein particles (Fielding & Fielding, 1996). The protein composition of a lipoprotein particle largely specifies the metabolism of its lipids (ibid.). Apoprotein molecules self-associate by clustering their hydrophobic surfaces together. This allows apoproteins, except for apo B, to exchange between lipoprotein particles and to interact with opposite charges on enzymes and receptor proteins (Davis & Vance, 1996, Fielding & Fielding, 1996). Types of apoproteins include apo A1, apo A2, apo C, and apo E (ibid.).

The major plasma lipoproteins are usually classified according to density (Davis & Vance, 1996, Fielding & Fielding, 1996). Since lipids have lower densities than proteins, lipoproteins with lower lipid/ protein ratios have higher densities and vice versa

(ibid.). There are two main classes of lipoproteins (see Figure 2.3.). The first consists of particles whose primary function is to deliver lipids (mainly TG) from the liver or intestine into the peripheral, extrahepatic tissues (Fielding & Fielding, 1996). Chylomicrons which contain principally TG are the largest and most lipid-rich particles (Davis & Vance, 1996). They are secreted by the intestine and are abundant in plasma only after a meal (Davis & Vance, 1996). Chylomicron TG originates from dietary long-chain fatty acids (Fielding & Fielding, 1996). These fatty acids are reesterified in the mucosal cells prior to secretion into the lymph (Fielding & Fielding, 1996). Following lipolysis, the chylomicron remnant, which has lost 80-90% of its TG, is avidly cleared and degraded by the liver (Fielding & Fielding, 1996; Rosenson, Frauenheim, & Tangney, 1994). The smaller lipid core of the chylomicron remnant then releases excess surface components that are used for the formation of HDL (Rosenson et al., 1994).

Very low density lipoproteins (VLDL) contain large concentrations of TG and moderate concentrations of phospholipids and cholesterol (Rosenson, 1994). VLDL TG originates in the liver and is mainly synthesized from fatty acids produced from acetate units of dietary carbohydrate (Fielding & Fielding, 1996; Guyton, 1986; Rosenson et al., 1994). Thus the size and lipid composition of both VLDL and chylomicrons vary according to nutritional status (Davis & Vance, 1996). Once VLDL has lost most of its TG via lipolysis to the peripheral tissues, some of their remnants are returned to the liver, endocytosed and catabolized (Fielding & Fielding, 1996). Others (about half) are further modified by losing most of their remaining TG, and apo E and remain in the circulation as low density lipoproteins (LDL) (Fielding & Fielding, 1996; Havel & Kane, 1995; Rosenson et al., 1994). Functionally VLDL, IDL, and LDL particles form a continuum of decreasing size and increasing density derived from lipolysis of TG, principally by lipoprotein lipase (Davis & Vance, 1996; Fielding & Fielding, 1996; Rosenson et al., 1994).

High density lipoproteins (HDL), the other class of lipoproteins, are a diverse population of particles both in structure and formation that transport lipid (mainly cholesterol) from peripheral tissues to the liver (Davis & Vance, 1996; Fielding & Fielding, 1996). The transport of cholesterol to the liver, called reverse cholesterol

transport, is one property of HDL that is considered to be antiatherosclerotic. Other properties of HDL include interference with LDL aggregation, a step that facilitates LDL uptake by endothelial cells; competition with LDL for endothelial-localized LDL receptors; facilitation of endothelial cell repair and proliferation, and maintenance of normal coronary artery vasoreactivity (Rosenson et al., 1994).

HDL contain about 50% protein and 50% lipids (Guyton, 1986). Its subfractions, HDL_2 and HDL_3, are the smallest of the lipoprotein classes and contain mainly cholesteryl esters in their cores (Havel & Kane, 1995). HDL cholesteryl ester may be delivered directly to the liver, or first transferred to apolipoprotein B-containing lipoproteins prior to hepatic uptake (Fielding & Fielding, 1996).

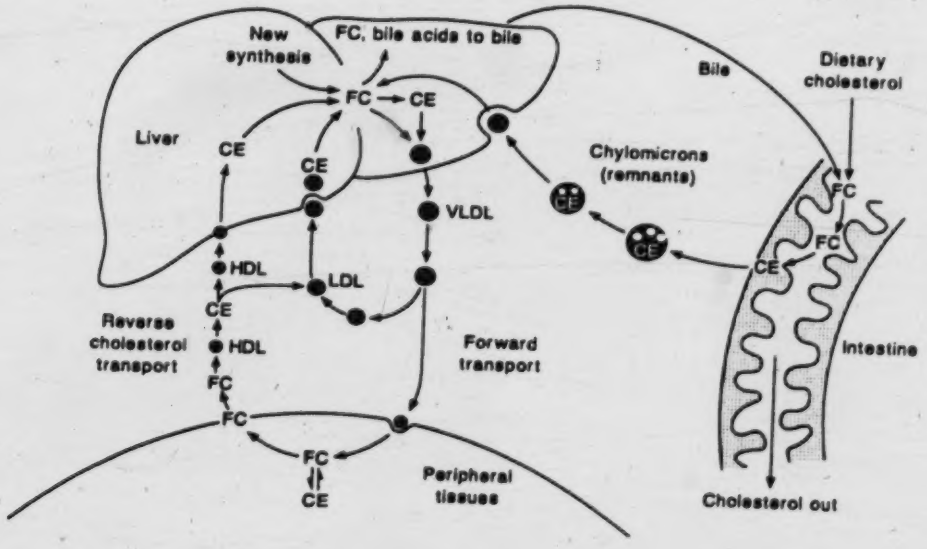


Figure 2.3. Major cholesterol transport pathways between liver and peripheral tissues. FC, free cholesterol; CE, cholesteryl ester; VLDL, very low density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein. Arrows indicate the direction of net transport. From "Molecular physiology of reverse cholesterol transport," by C.J. Fielding & P.E. Fielding, 1995, Journal of Lipid Research, 36, p. 212. Copyright 1995 by Lipid Research, Inc. Reprinted with permission of the author.

Lipoprotein Lipase (LPL).

LPL is an acylglycerol hydrolase synthesized mainly in the parenchymal cells of smooth and adipose tissue. Once synthesized, LPL is transported to the vascular surface of these tissues (Fielding & Fielding, 1996). The level of LPL activity in individual tissues is a function of nutritional and physiological stress that affect TG uptake, such as fasting and exercise (Kinnunen, 1984). Hydrolysis of VLDL and chylomicron TG occurs at the capillary endothelial surface through the action of LPL and monoacylglycerol lipase (Fielding & Fielding, 1996, Kinnunen, 1984).

$$\text{TG} \xrightarrow[H_2O\ \ FA]{LPL} \text{sn-2,3-diacylglycerol} \xrightarrow[H_2O\ \ FA]{LPL} \text{2-monoacylglycerol} \xrightarrow[H_2O\ \ FA]{\text{P-MGH}} \text{glycerol}$$

where LPL is lipoprotein lipase, P-MGH is monoacylglycerol lipase, H_2O is water, and FA is fatty acid (Kinnunen, 1984).

Lipoprotein-derived fatty acids cleared by adipose tissue are reesterified forming a reservoir used during fasting when hormone-sensitive lipase within the adipocyte promotes the release of unesterified fatty acids back into the circulation (Fielding & Fielding, 1996). Fatty acids used by muscle represent an immediate energy source.

Regulation of capillary LPL activity in adipose tissue and muscle is different (Felber et al, 1993). In the postprandial state, elevated insulin activates adipose tissue LPL to increase FFA removal from plasma and deposition of TG in adipocytes. In contrast, the activity of LPL associated with capillaries of skeletal muscle is suppressed by feeding and increased in the postabsorptive state (ibid.). The differential regulation of adipose tissue and skeletal muscle LPL thus directs VLDL and chylomicron TG to adipocytes for storage in the postprandial state and to muscle cells for oxidation in postabsorptive state (ibid.).

Kinetics of the LPL reaction. As VLDL and chylomicrons pass down their delipidation cascade, partially catabolized intermediates formed as a result of LPL

activity are detected in the circulation indicating that lipolysis does not result from a single binding event (Fielding & Fielding, 1996). Rather, there must be repeated dissociation and rebinding, during which lipoprotein TG is catabolized, apo C2 gradually lost, and LPL catalytic rate decreased (ibid.). During this process, TG-rich molecules are reduced and excess surface components including phospholipid, unesterified cholesterol and apoproteins A, C, and E are transferred to HDL (Rosenson et al., 1994).

Reverse cholesterol transport.

Reverse Cholesterol Transport (RCT) is the term used to describe a pathway by which cholesterol in extrahepatic tissues is transported via the plasma to the liver from which it may be recycled to extrahepatic tissues or excreted into the intestine in bile (Barter & Rye, 1996; Fielding & Fielding, 1995; Loh & Tan, 1996) (see Figure 2.4). This process is felt to facilitate the removal of excess intracellular cholesterol from atherosclerotic plaques (Rosenson et al., 1994). RCT involves several regulated steps mediated by the plasma apoproteins and the enzymes, lecithin:cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein (CETP), and HL (Loh & Tan, 1996).

Lecithin: cholesterol acyltransferase (LCAT).

Cholesterol removed from peripheral tissues by nascent HDL is esterified by LCAT (secreted in the liver) in plasma (Fielding & Fielding, 1996) (see Figure 2.4.). The optimal substrate for LCAT is the discoidal HDL containing 3-4 apo A1 polypeptides per particle (Fielding & Fielding, 1996). Also, LCAT is more effective with apo A1 HDL than apo A1, A2 HDL particles (Barter & Rye, 1996; Fielding & Fielding, 1996). LCAT activity decreases as cholesteryl ester accumulates in the growing spherical HDL particle (Fielding & Fielding, 1996).

Cholesteryl ester transfer protein (CETP).

Cholesteryl esters formed by LCAT are exchanged for TG with VLDL, IDL, and LDL under the influence of cholesteryl ester transfer protein, CETP (Fielding & Fielding, 1996; Wooley & Petersen, 1994) (see Figure 2.4.). The CETP reaction expands the

capacity of plasma to clear cholesteryl esters, by using VLDL, IDL, and LDL particles to carry cholesteryl ester back to the liver, when most of TG content has been lost to lipolysis (ibid.).

Hepatic Lipase (HL).

The role of HL remains somewhat enigmatic (Wooley & Petersen, 1994). HL appears to be synthesized in liver parenchymal cells (Kinnunen, 1984). After secretion, HL becomes bound to receptors on the surface of the liver (Kinnunen, 1984). HL appears to participate in the hydrolysis of HDL-TG, the hydrolysis or passive transfer of phospholipids, the selective transfer of HDL cholesteryl esters to the liver in the conversion of HDL_2 to HDL_3, the loss of apo A1 from the newly decreased surface of the lipoprotein particle, and may also be involved in the terminal stages of delipidation of chylomicron and VLDL remnants (Fielding & Fielding, 1996; Kinnunen, 1984; Mowri, 1996; Wooley & Petersen, 1994) (see Figure 2.4). In vivo, the activity of HL with HDL TG produces small dense HDL particles and free apo-A-1 which can then re-circulate in the reverse cholesterol transport pathway (Fielding & Fielding, 1996).

The Apo A-I Cycle.

The hypothetical cycle in which pre-β-migrating HDL particles promote cholesterol efflux is as follows: 1) apo A-I, present in nascent HDL or dissociated from spherical, α-migrating HDL as a consequence of a remodelling of the particle by factors such as HL, 2) a proportion of the lipid-free or lipid-poor apo A-I transfers from plasma to the interstitial space, 3) apo A-I recruits phospholipids from cell membranes to form discoidal pre-β-1 HDL, 4) pre-β-1 HDL accept cholesterol from cell membranes and are converted into larger discoidal pre-β-2 HDL, 5) pre-β-2 HDL are transported via lymphatics to plasma where they bind LCAT, and 6) LCAT-mediated esterification of cholesterol provides the particle with a core of cholesteryl esters, converting it into a spherical, α-migrating HDL thus completing a cycle that transfers cell cholesterol into the plasma (Barter & Rye, 1996).

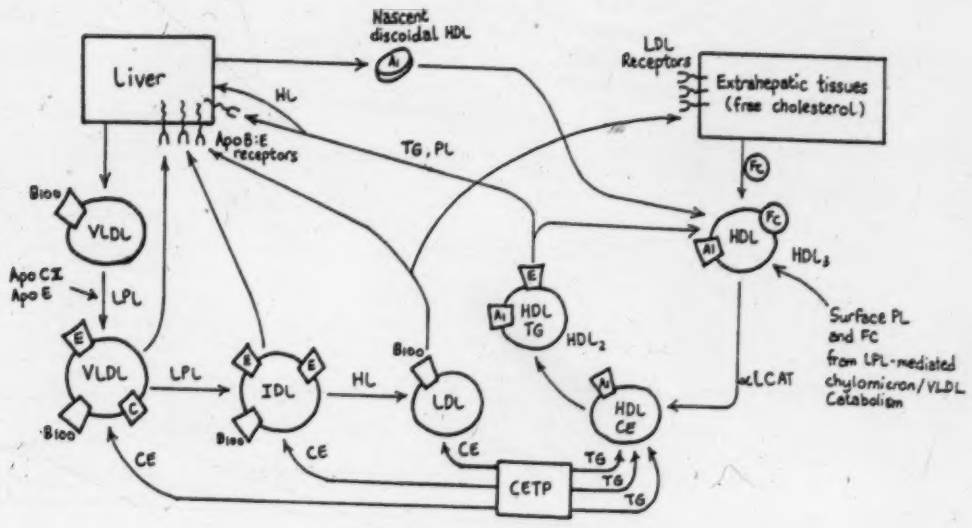


Figure 2.4. Schematic diagram of reverse cholesterol transport. AI, Apo A-I; B 100, Apo B-100; C, ApoC; CE, Cholesteryl ester; CETP, Cholesteryl ester transfer protein; E, ApoE; FC, Free cholesterol; HL, Hepatic lipase; αLCAT, Alpha-lecithin: cholesterol acyltransferase; LPL, Lipoprotein lipase; PL, phospholipids; TG, triglycerides. From "Reverse cholesterol transport: Its contribution to cholesterol catabolism in normal and disease states," by K-C. Loh and M-H. Tan, 1996, Canadian Journal of Cardiology, 12(10), p. 946. Copyright 1996 by Pulsus Group, Inc. Reprinted with permission of the author.

Removal of LDL from the Circulation.

In addition to endogenous synthesis, cells are supplied with cholesterol via receptor-mediated endocytosis of LDL (Schneider, 1996). The following section describes this process.

The LDL receptor pathway.

First, the lipoprotein particle binds to one of the estimated 15 000 LDL receptors on the surface of a cell (Schneider, 1996). LDL receptors are not distributed evenly on the cell surface, but concentrated into specialized regions of the plasma membrane, clathrin-coated pits. These coated pits contain other receptors in addition to LDL receptors, but LDL bind only to their own receptors. Next, the receptor/LDL complex undergoes endocytosis by rapid invagination of the coated pit, which culminates in pinching-off of the pit into the interior of the cell. Once in the cell, the coat is rapidly removed and undergoes acidification of its interior and fusion with other uncoated endocytic vesicles. Transiently, LDL and the receptor are found in smooth vesicles termed endosomes; therein the lipoprotein particle dissociates from the receptor due to the acidic environment. Subsequently, LDL is delivered to lysosomes, where it is degraded, and the receptor returns to the cell surface (Schneider, 1996).

The cholesterol liberated by the lysosomal hydrolysis of LDL cholesteryl esters, or possibly an oxidized sterol(s) derived therefrom, mediates a complex series of feedback control mechanisms that protect the cell from overaccumulation of cholesterol (Schneider, 1996). First, LDL-derived sterols suppress the activities of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) synthase, and HMG-CoA reductase, two key enzymes in cellular cholesterol biosynthesis. Second, the cholesterol activates a cholesterol-esterifying enzyme called acyl-CoA:cholesterol acyltransferase which allows the cells to store excess cholesterol in the form of cholesteryl ester droplets. Third, the synthesis of new LDL receptors is suppressed, preventing further cellular entry of LDL and thus cholesterol overloading.

This receptor-mediated regulation system coordinates intra- and extra-cellular sources of cholesterol (Schneider, 1996). Human fibroblasts and other mammalian cells are able to synthesize cholesterol from acetyl-CoA and therefore can subsist in the absence of lipoproteins. However, when LDL is available, cells suppress their own synthetic activity and use the LDL receptor to import LDL. Thus, the cholesterol level is maintained constant within the cell regardless of large fluctuations outside the cell. In vivo, the main task of LDL receptors is to supply cells cholesterol and mediate the

removal of cholesterol-rich lipoprotein particles from the bloodstream. Disrupted LDL receptor function disturbs this balance and has severe clinical consequences. Oxidation of LDL can result in the overaccumulation of cholesterol in cells by scavenger receptors which, unlike the LDL receptor, are not down-regulated by increased cell cholesterol content. Insufficient removal of cholesterol by circulating HDL particles can also result in an imbalance in cellular cholesterol content (Schneider, 1996).

Atherosclerosis.

Atherosclerosis is a complex process that is characterized by the accumulation of modified LDL, local inflammatory and immune responses, and reduced nitric oxide bioavailability within the arterial wall (Kinlay & Ganz, 1997). The result is an overaccumulation of lipid, mostly free and esterified cholesterol, in the wall of blood vessels (Schneider, 1996). The overaccumulation of lipid is associated with abnormalities of lipid metabolism and any factor (physical abrasion, arterial pressure) that injures the arterial wall (Guyton, 1986). Furthermore, it has been suggested that fibrin formation may be involved in the development of atherosclerotic lesions and thus has an impact on atherosclerotic plaque formation (Buemann & Tremblay, 1996). Moreover, fibrin is positively correlated with obesity, insulin resistance, and plasminogen activator inhibitor (inhibits tissue plasminogen activator) which are risk factors for CVD (Buemann & Tremblay, 1996).

The accumulation of cholesterol in atheromata leads to the so-called "fatty streak", the earliest recognizable lesion (Ross, 1993).The fatty streak (Ross, 1995) is an aggregation of lipid rich macrophages and T lymphocytes within the innermost layer of the arterial wall, the tunica intima (Ross, 1993). These lesions become intermediate lesions when layers of macrophages and smooth muscle cells from tunica media appear within the intima, and in turn develop into the more advanced complex lesions called fibrous plaques (Ross, 1993, 1995).

Fibrous plaques are covered by a dense cap of connective tissue with embedded smooth muscle cells that usually overlays a core of lipid and necrotic debris (Lee & Libby, 1997; Ross, 1993). Plaques can be stable or vulnerable to rupture (Kinlay & Ganz,

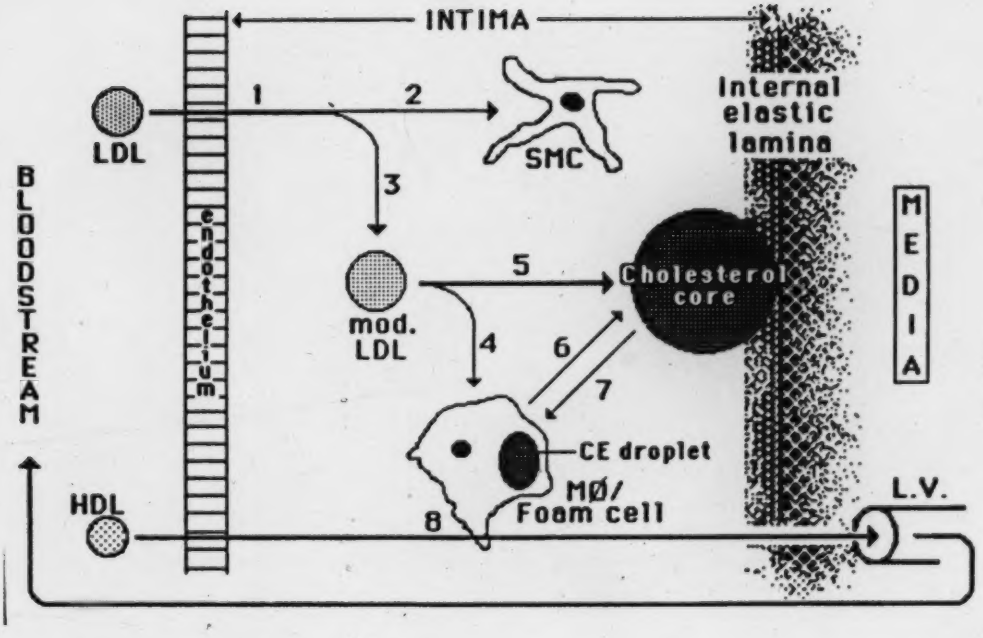
1997). There are two possible ways to make the plaque structure unstable. Compared to stable plaques, vulnerable plaques have a large lipid-rich core which is several orders of magnitude softer than the thinner fibrous cap, with a semifluid consistency at body temperature (Lee & Libby, 1997). This mechanical property is likely to be a critical factor in determining plaque stability; the softer the lipid core, the more stress the fibrous cap must bear (Lee & Libby, 1997). Vulnerable plaques also contain a high concentration of inflammatory cells and activated smooth muscle cells. The inflammatory cells include monocyte-derived macrophages and lymphocytes (Kinlay & Ganz, 1997). These inflammatory cells as well as smooth muscle cells are activated by cytokines in the intima to release degradative enzymes, including metalloproteinases, that degrade the extracellular matrix and weaken the fibrous cap, making it vulnerable to rupture (Kinlay & Ganz, 1997; Knox, Sukhova, Whittemore, & Libby, 1997; Mach, Schönbeck, Bonnefoy, Pober, & Libby, 1997). Pathological studies have examined shear stresses at various parts of plaques and found increased stresses at the shoulders of plaques where inflammatory cells are found in high numbers (Kinlay & Ganz, 1997). Thus the sites where the fibrous cap is weakened by inflammatory cells coincide with the areas that receive the greatest stresses and where plaque rupture is most often observed (Kinlay & Ganz, 1997).

As plaques rupture, the resulting thrombus formation at the site of injury can lead to complete occlusion of the artery, myocardial infarction, and often sudden death (Rosenson et al., 1994; Ross, 1993). This response to endothelial injury which initially begins as a protective mechanism and ultimately results in damage to tissue served by the artery is referred to as the "response to injury hypothesis" (Ross, 1993, 1995) (see Figure 2.5).

In addition to modified LDL and the inflammation process, atherosclerosis also reduces nitric oxide. Nitric oxide, which is produced by the vascular endothelium, diffuses from the endothelial cell to the vascular smooth muscle and increases relaxation of smooth muscle (vasodilation) in response to acetylcholine (Kinlay & Ganz, 1997). Further studies have shown that nitric oxide is also responsible for counteracting the vasoconstricting effect of acetylcholine on vascular smooth muscle (ibid.). Therefore

when nitric oxide is reduced, atherosclerotic arteries tend to constrict due to the unopposed effect of acetylcholine on vascular smooth muscle (ibid.). This increases the likelihood or contribution to inflammation in plaques because of increased adherence and migration of monocytes, formation of lipid-laden macrophage, and increased expression of plasminogen activator inhibitor and tissue factor especially in areas surrounding a lipid core (Selwyn, Kinlay, Libby, & Ganz, 1997). Investigations have shown that reduced nitric oxide, endothelium-dependent dilation to acetylcholine and serotonin, and flow in coronary and brachial arteries are associated with a number of factors. These include increased serum cholesterol, increased LDL, decreased HDL, and the presence of risk factors for CVD such as male gender, increasing age, smoking, high blood pressure, and diabetes mellitus (Adams et al., 1998; Kinlay & Ganz, 1997; Selwyn et al., 1997). Small dense LDL particles and larger LDL particles are particularly associated with reduced nitric oxide, since they are more susceptible to oxidation and overproduction of oxygen-derived free radicals which may combine with nitric oxide to decrease the bioavailability of nitric oxide and induce endothelial vasomotor dysfunction (Adams et al., 1998; Kinlay & Ganz, 1997). However, decreasing total cholesterol and LDL cholesterol can improve endothelial vasomotor function over a period of weeks to months (Kinlay & Ganz, 1997). This results in greater vasodilation of vascular smooth muscle and increases blood flow in coronary vessels (ibid.).

Figure 2.5. The intimal traffic of cholesterol: schematic representation of processes leading to the formation of foam cells and extracellular cholesterol core. (1) Plasma LDL particles enter the intimal layer by crossing the endothelium. (2) LDL particles are bound to LDL receptors on the surface of smooth muscle cells (SMC) and are degraded within them. (3) Some of the non-degraded LDL becomes extracellularly modified by SMC's mast cells, and macrophages, resulting in particles not recognized by the LDL receptor (mod. LDL), (4) Macrophages (MØ) remove modified LDL particles by scavenger receptors and are transformed into cholesteryl ester (CE)-loaded foam cells. (5) Some of the modified LDL might escape scavenging and form an extracellular cholesterol core trapped in the intima by the internal elastic lamina. (6) Some foam cells die, and their cholesteryl droplets fuse with the cholesterol core. (7) Parts of the cholesterol core may become phagocytosed by macrophages or foam cells. Plasma HDL's, possibly pre-beta HDL particles, cross the endothelium; due to their small size are more mobile than LDL particles, and (8) interact with foam cells where they become loaded with cholesterol (this constitutes the initial step of reverse cholesterol transport). The HDL particles then cross the intimal layer and reach the lymphatic capillaries of the medial layer, to be ultimately conveyed back to the bloodstream. The formation of foam cells and cholesterol core (characteristic of an atheroma) are due to an imbalance between cholesterol influx via LDL and cholesterol efflux via HDL. Fatty streaks are clusters of foam cells without the extracellular cholesterol core found in atheromata. Reprinted from "Removal of lipoproteins from plasma," by W.J. Schneider, 1996, in D.E. Vance & J. Vance (Eds.), Biochemistry of lipids, lipoproteins and membranes p. 536. Copyright 1996 with permission from Elsevier Science B.V.


INTIMA
Internal elastic lamina
LDL
1
2
SMC
3
BLOODSTREAM
endothelium
mod. LDL
5
Cholesterol core
MEDIA
4
6
7
CE droplet
MØ/ Foam cell
8
HDL
L.V.

Part 2: CVD in SCI

> As time passes, the causes of death among individuals with SCIs move away from the classic causes of death in SCIs such as renal failure, and begin to approximate the causes of death of the nondisabled population. Of note, however, is that these deaths are occurring at ages somewhat lower than one would expect within the general nondisabled population (Whiteneck, 1993, pp 32-33).

According to the British Study (1991), which represents that largest investigation conducted of persons more than 20 years post-SCI, cardiovascular deaths were the most frequent cause of death among persons more than 30 years post-injury (46% of all deaths) and among people over 60 years of age (35% of all deaths) (Whiteneck et al, 1992). In concert with other research in this area, this study found that cardiovascular and respiratory deaths became more frequent with aging with a somewhat greater rate at most ages than the general population (Whiteneck et al., 1992; Bauman et al., 1992a; Geisler, Jousse, Wynne-Jones, Breithaupt, 1983). In another study, 77 people with SCI and 53 lower limb amputees were compared to a control group (Yekutiel, Brooks, Ohry, Yarum, & Carel, 1989). Results showed that 34% of people with SCI had hypertension, ischemic heart disease, or diabetes mellitus compared to 18.6% of controls (Yekutiel et al., 1989). Seventeen percent of people with SCI had ischemic heart disease compared with only 7% of controls (Yekutiel et al., 1989). While cardiovascular causes of morbidity and mortality to some extent may be related to autonomic dysfunction and diminished efficacy of the cardiovascular system, development of atherosclerosis and CVD may be accelerated by immobility, reduced HDL levels and physical inactivity (Bauman et al., 1992a, 1992b; Bauman & Spungen, 1994; Maki et al., 1995; Ragnarsson, 1993).

Reduced HDL

In the second report of the Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (NCEP, 1994) low HDL cholesterol is classified as a major risk factor of coronary heart disease, and recommends that HDL cholesterol be measured in initial risk assessment. This is especially important for people with SCI, as the cardioprotective HDL fraction may remain low even while the total cholesterol level is within normal limits (Tharion, Prasad, Gopalan, & Bhattacharji, 1998). A low HDL level has been identified as the primary risk factor for CVD in people with SCI (Bauman & Spungen, 1994; Krum et al., 1992, Yekutiel et al., 1989, LaPorte et al., 1983; Tharion et al., 1998). This predicts over 60% of the increased risk in the sedentary SCI population as compared to the nondisabled population (Brenes, Dearwater, Shapera, LaPorte, & Collins, 1986).

Reduced HDL levels were evident when researchers investigated the incidence of cardiac risk factors in 327 Israeli patients with SCI (aged 25-64) and compared them to 1.17-1.35 mmol/L reported in a survey on Australian able-bodied persons (Krum et al., 1992). A questionnaire assessment determining cigarette consumption, dietary habits, alcohol consumption, stress levels, physical exercise level, and family medical history was performed by 102 patients to assess cardiac risk. Also, body weight, recumbent systolic and diastolic blood pressures, serum cholesterol, lipid fractions, and serum glucose were measured. Results showed that dietary habits, serum cholesterol levels and smoking were similar, but diastolic blood pressure and body weight were significantly lower in the SCI population. The net result was a risk factor score for both males and females below the fiftieth percentile for all age groups in people with SCI, yet the incidence of ischemic heart disease, cerebrovascular accident (stroke) and hypercholesterolemia was similar in the two groups. Reduced HDL level (1.03-1.15 mmol/L) was the only risk factor that could account for an equal incidence of illness in the SCI population (Krum et al., 1992).

This finding was recently confirmed in a study where 58% of people with paraplegia and quadriplegia had reduced HDL levels (Tharion et al., 1998) and also in another study where 53% of persons with quadriplegia with desirable total cholesterol

had low HDL levels (below 0.91 mmol/L) as compared to only 10% of controls (Shetty, Sutton, Rudman, & Rudman, 1992). In this latter study, HDL_2 (0.32 mmol/L) and HDL_3 (0.38 mmol/L) were significantly decreased in persons with quadriplegia as compared to controls (0.56 mmol/L and 0.53 mmol/L, respectively)(Shetty et al., 1992). The authors concluded that quadriplegia is associated with reduced levels of HDL and its subfractions which partly explains the higher incidence of coronary artery disease (Shetty et al., 1992). Similarly, Bauman et al. (1992b) showed 48% of persons with paraplegia (16 years post injury) had HDL levels less than 0.9 mmol/L. Of these persons with paraplegia, 20% had HDL levels less than 0.77 mmol/L. In addition, 63% of persons with paraplegia aged 54 and with an average 17 years post injury had latent coronary heart disease when radionuclide myocardial perfusion imaging was performed after ACE exercise (Bauman et al., 1992b). Unfortunately, there were no controls in this study.

Only one study opposes these findings (Cardús, Ribas-Cardús, & McTaggart, 1992). Their study was designed to compare blood levels of total cholesterol and lipoproteins, LDL and HDL of 96 men with SCI (46 persons with paraplegia and 50 with quadriplegia) with a non disabled population. These authors also investigated the relation of any abnormal finding to age at onset of the SCI, duration of injury or level of the lesion. Results showed that people with SCI did not have higher levels of cholesterol or LDL, nor lower levels of HDL. Blood levels of HDL and LDL did not seem to be related either to the duration of the injury or to the lesion level. They concluded that the disagreement between their findings and those of previous reports were that the number of subjects in previous reports were generally small and the average values were computed over ages that spread over large ranges. Also some studies were performed in the early state of the disability and persons with severe associated clinical complications.

Although Cardús et al. state that sample size may affect results, recent studies (Krum et al., 1992; Bauman et al., 1992b) have used similar number of subjects ($\geq$100) and results have shown reduced HDL levels. Also, this study's limitations were that apart from duration of injury and lesion level there are other factors (ie. physical activity and diet) not included in their research, that affect HDL levels. Some of these factors are discussed below.

Etiology of reduced HDL levels in people with SCI.

Although many mechanisms for reduced HDL have been speculated, they have yet to be proven in research (Loh & Tan, 1996). However, changes in diet, activity, body composition, and lifestyle must all be considered as causative factors for this abnormality in lipid profile (Shetty et al., 1992).

The sympathetic nervous system (SNS).

SCI results in varying degrees of decentralisation of the sympathetic, as well as the parasympathetic nervous system, depending on the completeness of injury (Karlsson, 1997). Cardiovascular, thermoregulatory, gastrointestinal, urinary, and reproductive systems are affected. The decentralisation of the SNS also affects metabolic regulation and results in disturbed glucose regulation accompanied by a reduction in blood pressure, an absent increase in EP, and NE and lack of neuroglycopenic symptoms. Since EP and NE are powerful stimulants of lipolysis and glycolysis, and people with SCI have a disrupted release of these stimulants, people with SCI are susceptible to hypoglycemia and absent or decreased lipolysis, decreased FFA uptake, and decreased HDL formation compared to the nondisabled population with stress or physical activity (Karlsson, 1997).

Physical inactivity.

Individuals with SCI most often become injured at a young age and lead physically inactive lives (Mohr et al., 1997; Dallmeijer et al., 1997; Ragnarsson et al., 1991). Physical inactivity is worsened by the fact that transportation and activities of daily living performed in a wheelchair do not require sufficient energy expenditure throughout the day to produce training responses (Hjeltnes & Vokac, 1979; Janssen, van Oers, van der Woude, & Hollander, 1994; Mollinger et al., 1985). This decrease in energy expenditure leads to increased fat mass, weight gain and obesity in the SCI population (Kocina, 1997; Ragnarsson et al., 1991; Maki et al., 1995).

Increased fat mass is one of the risk factors for insulin resistance (Björntorp, 1990; Després et al., 1990) for abdominal adipose tissues have an exceedingly sensitive system for the mobilization of FFA due to a preponderance of β-adrenergic receptors and

α-adrenergic inhibition (Kissebah & Peiris, 1989). This increased mobilization of FFA in the circulation inhibits insulin binding action, decreases the number of insulin receptors and decreases clearance by the liver (Björntorp, 1990), and reduces the formation of HDL in the circulation.

Reduced muscle mass.

Paralysis of the lower and upper extremities as a result of SCI decreases muscle mass in people with SCI as compared to nondisabled people in spite of normal body weight (Bauman & Spungen, 1994; Karlsson, 1997; Kocina, 1997). However, the most striking difference between normal and paralyzed muscle is the absence of fibres containing myosin heavy chain (MHC) Type I/slow twitch fibres (Andersen et al., 1996). Andersen et al. (1995) reported that 37.2% of the paralyzed muscle fibres contained only MHC Type IIb, 21.2% only MHC Type IIa, 40.7% co-expressed MHC Type IIb and IIa/ fat twitch oxidative fibres, and 0.5% contained MHC Type I as compared to 4%, 25%,12%, and 50% respectively in nondisabled controls. This occurs in concert with a decrease in the activity of the oxidative enzyme succinic dehydrogenase, decreased muscle fibre diameter and increased MHC Type IIb/ fast twitch glycolytic fibres (Andersen, Hamman, Savage, Saad, Laws, Kades et al., 1995; Andersen et al., 1996; Burnham et al., 1997). As slow twitch fibres in humans are aerobic, oxidative, and are able to metabolize FFA liberated by LPL from circulating TG-rich lipoproteins to provide energy stores during prolonged activity (Tikannen, Naveri, & Harkonen, 1996), a decrease in this fibre type would decrease the uptake of FFA in muscle and decrease their clearance in the blood. Consequently, TG and TG-rich lipoproteins would rise, HDL cholesterol levels would decrease, and the risk of CVD would increase (Bauman & Spungen, 1994).

Decreased muscle mass not only affects fatty acids, but also glucose uptake. In healthy, innervated muscle, glucose uptake is facilitated by two pathways: insulin mediated and non-insulin mediated (muscle contraction). Once muscle is denervated, as with SCI, the muscle quickly becomes insulin resistant (Burant, Lemmon, Treutelaar, & Buse, 1984; Felber et al., 1993; Turinsky, 1987). Two studies showed that after 3-6 hours

post-denervation in rat muscle, insulin reduced its uptake of a glucose analogue by 20-58% in MHC Type I fibres and Type IIa fibres, but not MHC Type IIb fibres. Three to 17 days later, the Type I fibres did not respond to insulin stimulation, whereas MHC Type II fibres responded but the insulin induced increment of glucose decreased 24-68% compared to contralateral innervated leg (Burant et al., 1984; Turinsky, 1987). Authors concluded that 1) the effect of denervation depended on muscle fibre population and 2) the decreased response to insulin leading to impaired insulin-mediated disposal of glucose or insulin resistance of the muscle, was caused by a cellular energy defect (Turinsky, 1987) and a lack of nervous stimuli and/or contractile activity to modulate signal transmission by the occupied insulin receptor (Burant et al., 1984).

Glucose transporters.

Further research on insulin resistance was performed by Block et al. (1991). Block et al., who investigated GLUT1 and GLUT4 glucose transporter isoforms in denervated rat hindlimb muscle, found that after one day of denervation, GLUT1 and GLUT4 protein concentration were unchanged. However after three and seven days post-denervation, GLUT1, based on DNA, increased 60 and 90%, respectively, and GLUT4, decreased 50%. Data suggest that the insulin resistance of glucose transport early after denervaton did not reflect a decrease in total glucose transport number, however, decreased GLUT4 as a result of insulin resistance could contribute to insulin resistance after three days (Block et al., 1991).

Lipoprotein Lipase (LPL) Dysfunction.

Insulin resistance further complicates metabolism as LPL activity, which degrades TG into glycerol and FFA, is determined by insulin (Dearwater et al., 1986). When insulin is less efficient at controlling blood glucose, insulin increases, LPL decreases, and TG particles accumulate (LeBlanc, Nadeau, Boulay, & Rousseau-Migneron, 1979). Similar findings were reported by Bauman & Spungen in 1994 who found a direct correlation between plasma insulin and serum TG combined with lower HDL cholesterol levels in people with SCI.

Part 3. Exercise

Exercise reduces mortality and morbidity caused by atherosclerotic complications through both direct (cardiovascular) and indirect (risk factor modification) mechanisms (Goldberg, 1989). The incidence of heart disease is lower in the physically active compared to the sedentary part of the population, and the rate of heart disease is lower with higher levels of fitness (Andersen, 1995). Evidence shows decreases in TG, LDL, and blood pressure levels in people who exercise (Goldberg, 1989). More importantly, exercise increases serum HDL concentrations and reduces the risk of coronary atherosclerosis, although this mechanism is unclear (Loh & Tan, 1996). Furthermore, studies indicate a reduced risk of coronary heart disease in people who are physically active as compared to those who are sedentary (Després & Lamarche, 1994; Dallmeijer et al., 1997). One recent study showed that sport activity in people with SCI was the most significant determinant of HDL levels, explaining 17% of the variance (Dallmeijer et al., 1997). This reduced risk of coronary heart disease and resulting significantly reduced mortality rate are observed among physically active people with or without consideration of hypertension, cigarette smoking and extremes or gains in body weight (Paffenbarger, Hyde, Wing, & Hsieh, 1986; Dallmeijer et al., 1997).

Furthermore, exercise has the potential to reverse many of the factors that occur with SCI. It can increase physical activity of paralyzed muscle tissue, increase muscle mass and MHC Type I and IIa, increase basal metabolic rate, increase catecholamine secretion, increase energy expenditure by providing a means for large paralyzed muscles to become active, increase weight loss, increase insulin sensitivity, increase lipoprotein lipase, decrease glucose and FFA in the circulation and raise HDL levels. Some of these factors increase with exercise in general while others require the assistance of FES. Exercise and its benefits will be discussed first, followed by a section of FES and its reported benefits in people with SCI.

According to the dose-response relationship between exercise and prevention, the magnitude of benefit for any given increase in activity is greater for less active persons (Haskell, 1994). This relationship is also true with respect to HDL levels (Després &

Lamarche, 1994). Thus sedentary people with SCI have a great chance of increasing HDL levels due to their initial low values attributed to physical inactivity.

LPL and HL.

The observed increase in HDL particles in active people compare to sedentary people has much to do with LPL which allows chylomicrons to deposit TG into adipose and skeletal tissue. In this transformation, surface remnants are liberated and sequester to HDL lipoproteins (Chapman & Bruckert, 1996). This mechanism was investigated by researchers who discovered that post-exercise responses in HDL subfractions are related to the ratio of two enzymes; plasma LPL and HL activities, which change with physical activity level (Després & Lamarche, 1994; Stubbe, Hansson, Gustafson, & Nilsson-Ehle, 1983). Després and Lamarche (1994) created a model where LPL helps convert HDL_3 molecules to HDL_2 while HL converts HDL_2 particles to HDL_3. In sedentary persons LPL activity is reduced so HDL_2 particles are reduced and HL activity is enhanced so HDL_3 particles are increased. In physically active people, the mechanism is reversed. LPL activity is enhanced and HL activity is reduced so that there is an overall buildup of HDL_2 particles relative to HDL_3 particles (Després & Lamarche, 1994).

The increase in LPL and its effect on HDL was examined in one study where 18 subjects trained three to five times a week for twelve weeks at heavy intensity or moderate intensity (Stubbe et al., 1983). After six weeks, results showed 7% increases in HDL. This increase was attributed to 6% decreases in HL ($P<0.05$), and 50% increases in LPL activity at adipose tissue ($P<0.05$), while LPL in plasma and skeletal muscle did not change. After 12 weeks of training at moderate intensity, the most marked change was a 36% increase in the HDL_2 subclass leading to an elevation of the HDL_2/HDL_3 ratio by 18% (Stubbe et al., 1983). Therefore, the enzymatic response with training increases HDL_2 and decreases HDL_3 levels to subsequently increase plasma concentration of HDL (Després & Lamarche, 1994). However, perhaps the enzymatic response was not only due to physical activity but also to the level of intensity.

Effects of intensity on LPL activity.

Training or intensity level influence the activation of plasma LPL and HL. For example, Gordon and colleagues (1994) found post exercise increases in LPL activity after high and low intensity exercise. However, greater increases in LPL activity were found after the high intensity exercise (27%) as compared to low intensity exercise (24%) (Gordon et al., 1994).

The definition of high and low intensity and their effects on HDL levels were examined in eight people with SCI who trained with wheelchair ergometry exercise for 30 minutes, three times a week at low intensity (50-60%VO_2 max) and moderate intensity (70% VO_2 max) (Hooker & Wells, 1989). Results showed increased HDL levels and decreased TG and LDL levels occurred only in the moderate intensity group whereas blood lipid levels remained relatively unchanged in the low intensity group. Authors concluded that a minimal intensity of 70% VO_2 max was required to elicit a training effect (Hooker & Wells, 1989).

Two other studies also showed significant increases in HDL and decreases in LDL levels with increased exercise intensity (Rubinstein et al., 1995; Stein et al., 1990). Stein et al. investigated blood lipid and lipoprotein changes in forty-nine men with SCI after 12 weeks of cycle ergometer exercise at: 65%, 75%, and 85% of maximal heart rate (HR max). Results showed that HDL levels increased at 75% and 85% HR max, but not at 65% HR max. LDL levels decreased at 75% HR max. The authors concluded that a minimum of 75% HR max was required for optimal changes in both HDL and LDL levels (Stein et al., 1990).

Weight Loss and Energy Expenditure.

Weight is controlled by the amount of energy (caloric) consumption relative to the energy expenditure. If caloric consumption is greater than energy expenditure the net result is weight gain and vice versa. When weight is gained there are two ways to lose it, diet or exercise. Which is better?

Williams, Krauss, Vranizan, & Wood (1990) examined the effects of weight loss by caloric restriction (diet) and by caloric expenditure (exercise) on lipoprotein

subfraction concentrations in 155 moderately overweight men aged 30-59 over a one year period. The subjects were divided into three groups: a) exercise without caloric restriction; b) diet without exercise; and c) no change in either exercise or diet. People in the first group began with light calisthenics and a 25 minute walk, jog, or run, three times a week at 60-80% of maximal heart rate and finished the study jogging 40-50 minutes five days a week. People in the second group were to reduce their caloric intake but not the percentage of fat, carbohydrate or protein. Results showed that both the diet and exercise groups increased HDL_2 mass whereas the controls had no significant changes. Authors concluded that the difference in HDL_2 was not due to exercise or diet, but due to the resulting weight loss that was attained by these two means (Williams et al., 1990). Another study investigating aerobic exercise alone vs. aerobic exercise and weight loss in obese middle-aged men ($29.5 \pm 0.8\%$ kgm^{-2}) found that those who were in the latter group decreased TG by 17%, LDL by 8%, LDL/HDL ratio by 20% and increased HDL by 11% (Katzel., Bleecker, Rogus, & Goldberg, 1997).

Other research in men with obesity demonstrated that exercise at 60-80% intensity without weight loss increased HDL, LPL and decreased HL levels in persons with normal HDL levels, however, HDL levels were unchanged in those with initially low levels (<1.00mmol/L). Authors concluded that unchanged HDL levels were due to the inability to alter TG metabolism (Zmuda et al., 1998). In support of this finding, Nicklas, Katzel, Busby-Whitehead & Goldberg (1997) found that low HDL levels associated with obesity (31-37 kgm^{-2}) were due to increased TG-rich lipoproteins which caused HDL increases to be blunted with moderate intensity training.

However, 42 obese (30 ± 5 kgm^{-2}) men aged 60 ± 9 years who followed a nine month weight loss (10%) following the American Heart Association Step 1 Diet without exercise, decreased TG by 17%, TC by 4%, LDL by 7% and increased HDL by 15% (Dengel, Katzel, & Goldberg, 1995). Increases in HDL were attributed to significantly increased HDL_2 levels. Therefore, it seems that exercise in non-obese and even moderately obese men can increase HDL levels however obese individuals require weight loss to increase HDL.

Després and Lamarche (1994) reinforce that emphasis should not be placed on increasing VO_2 max through high intensity exercise but rather on producing a substantial increase in daily expenditure of energy that will eventually lead to weight loss and related improvements in carbohydrate and lipid metabolisms (Jennings, 1995) . According to Haskell (1994) the estimated increase in energy expenditure between the least active participants and those in a "moderate activity" category is 150-400kcal/day. This increase in energy expenditure would place people in the 500 to 3500 kcal/week range and roughly translates to a 24% reduction in risk of CVD death in sedentary men who become active (Paffenbarger et al., 1986). This justifies the necessity of exercise in reducing the risk for CVD (Brenes et al., 1986).

Functional Electrical Exercise for Persons with SCI.

As previously discussed, exercise provides an opportunity for people with SCI to prevent CVD and diabetes. The most common way for people with paraplegia to improve physical fitness has been participation in different wheelchair sports which involve the use of the upper limbs such as racing, basketball, tennis, swimming, canoeing, and ACE (Ragnarsson et al., 1991). Unfortunately, these means of fitness training are not as accessible for people with quadriplegia who have reduced upper body muscle mass (Faghri, Roger, Glaser, & Figoni, 1992; Ragnarsson et al, 1991). In addition, regular prolonged and perhaps excessive upper extremity exercise superimposed on daily strain of manual wheelchair propulsion and self-care, may accelerate the development of degenerative conditions of the upper extremities such as osteoarthritis, tendinitis, bursitis, and carpal tunnel syndrome (Ragnarsson, 1988; Ragnarsson et al., 1991). Moreover, upper body exercise uses a small percentage of the total body musculature in the body, which has no effect on the large mass of paralyzed muscles in the legs (Ragnarsson et al., 1991) that are insulin resistant and less efficient at clearing FFA and glucose from the circulation.

FES-assisted exercise, which uses electrical current to produce sequential muscle contractions via superficial electrodes placed on large muscle groups such as the quadriceps, provides a solution to the problem of physical inactivity of paralyzed muscle

in the legs of people with SCI. There are a number of FES-assisted exercise modalities available, including FES leg strengthening, FES leg cycling ergometry (FES-LCE), FES rowing, and HE exercise. HE exercise combines rhythmic FES induced contractions in the lower limbs (FES-LCE) with ACE (cranking mounted bike pedals with the arms) in the upper limbs.

Benefits of FES-Assisted Exercise.

The benefits of FES include: a) use of large muscle groups that would otherwise be inactive; b) increased cardiac muscle; c) improved circulation and increased cardiopulmonary fitness; d) enhanced rehabilitation; and e) increased catecholamine levels.

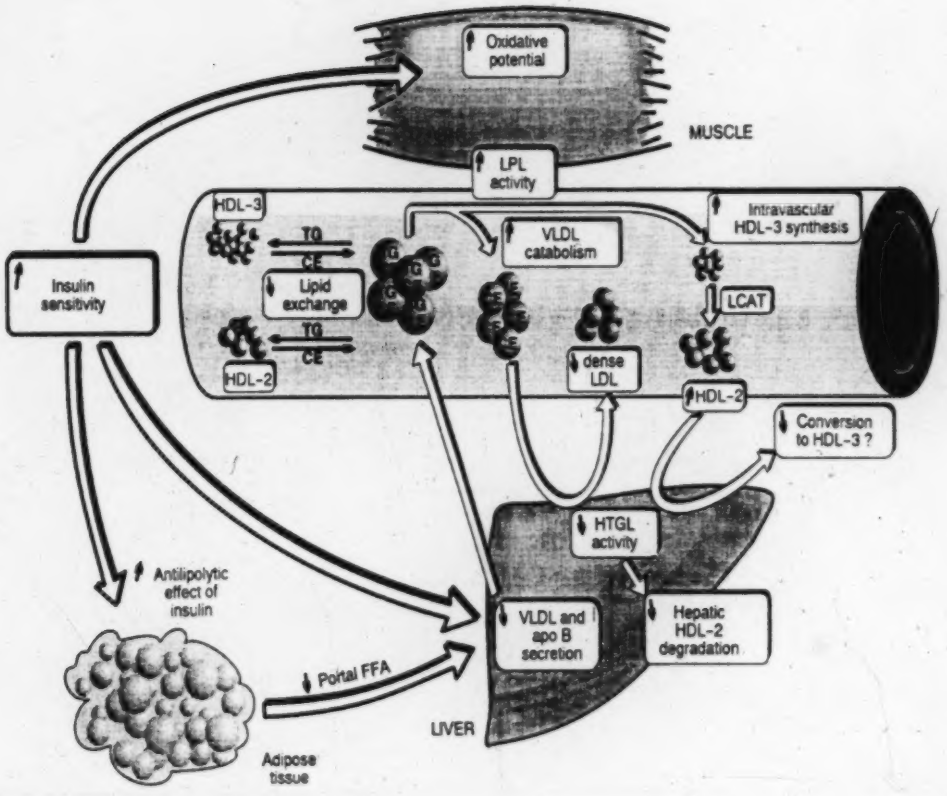
Use of large muscle. Muscle inactivity due to paralysis has been shown to cause histochemical changes in MHC fibres causing them to exhibit characteristics more like fast twitch (Figoni et al., 1990). Training paralyzed human skeletal muscle with FES can reverse these changes. Studies show that FES assisted exercise training can switch equal amounts of MHC Type IIa and MHC Type IIb expression to almost a total dominance of MHC Type IIa after six months of training (Andersen et al., 1996). Apparently the long term FES-training reduces both the number of fibres containing MHC Type IIb, and the number of fibres co-expressing MHC Type IIa and IIb to approximately the number observed in normal muscle. Moreover, FES-training increases the number of fibres containing only MHC IIa to a greater number than that observed under normal conditions (Andersen et al., 1996). Increasing oxidative fibres has been suggested to increase HDL levels through their high oxidative energy metabolism and surrounding capillaries which enable them to metabolize fatty acids liberated by LPL from TG-rich lipoproteins (Tikannen et al., 1996). LPL function is induced by insulin and is high in anabolic situations (Havel & Kane, 1995). Since insulin is one determinant of LPL activity (Dearwater et al., 1986), when insulin is less efficient in controlling blood sugar, LPL stimulation is less efficient (LeBlanc et al., 1979). Therefore, with exercise and its concomitant decrease in insulin resistance, it is anticipated that insulin will be more

efficient at controlling blood sugar and LPL more efficient at breaking down substrates to be stored in muscle; accordingly HDL levels will rise (see Figure 2.6.).

Although an exact physiological role of HL has not been established, research indicates that training and reduces the HL activity (Gorski, Oscai, & Palmer, 1990; Després & Lamarche, 1994). A decrease in HL reduces the production of TG and increases the production of HDL cholesterol by the liver (HDL_3), and decreases the conversion of HDL_2 to HDL_3 (Després & Lamarche, 1994; Gorski et al., 1990). Research has also shown that HL activity may be affected by diet in that an increase in carbohydrates increases HL and an increase in fat decreases HL (Gorski et al., 1990). If this is true, then it is possible that this is the way in which fat increases HDL, particularly HDL_2.

Training paralyzed muscle with FES has shown to significantly improve voluntary isometric strength, isometric endurance of the quadriceps, and muscle grading of the quadriceps and biceps femoris. Also, cross sectional areas of the quadriceps and total thigh muscle have increased after three months of FES-LCE three times per week in 12 persons with lesions C5-T12 result (Sloan et al., 1994). This is very significant for a variable portion of glucose intolerance (insulin resistance) associated with paralysis is a consequence of the loss of the primary site for meal deposition (Bauman et al., 1994).

Figure 2.6. Overview of some potentially important factors involved in the adaptation of lipid transport and plasma lipoprotein levels to endurance-exercise training. An important correlate of the lipoprotein changes is the improved in-vivo insulin sensitivity that is observed in endurance-training individuals. This adaptation improves the antilipolytic effect of insulin on adipose tissue as well as the insulin-stimulated glucose transport in the skeletal muscle. The resulting reduction of plasma insulin levels combined with reduced portal delivery of FFA to the liver leads to decreased hepatic VLDL and apolipoprotein B secretion. Furthermore, the reduced fasting plasma TG levels of endurance trained subjects also appear to result from a more efficient catabolism of TG-rich lipoproteins as LPL is elevated in adipose and muscle as well as in post-heparin plasma. The resulting reduced VLDL levels is associated with a decreased exchange of VLDL-TG for HDL and LDL cholesterol ester. The reduced TG levels observed in trained subjects also favour a decrease in the formation of small, atherogenic LDL particles. Furthermore, the elevated LPL activity of endurance-trained subjects increases the production of HDL precursors and a high LCAT activity may also be an important correlate of elevated HDL2 levels. Finally HL , which is high in sedentary obese individuals, is markedly reduced by endurance training. From "Low-intensity endurance exercise training, plasma lipoproteins and the risk of coronary heart disease," by J.-P. Després and B. Lamarche, 1993, Journal of Internal Medicine, 236, p. 16. Copyright 1994 by Blackwell Scientific Publications Ltd. Reprinted with permission from publishers.


Oxidative potential
MUSCLE
LPL activity
HDL-3
TG
CE
Lipid exchange
TG
CE
HDL-2
VLDL catabolism
Intravascular HDL-3 synthesis
LCAT
dense LDL
HDL-2
Conversion to HDL-3 ?
Insulin sensitivity
HTGL activity
Antilipolytic effect of insulin
VLDL and apo B secretion
Hepatic HDL-2 degradation
Portal FFA
LIVER
Adipose tissue

Increased cardiac muscle. Cardiac atrophy has been reported to occur in persons with quadriplegia who sustain extended periods of imposed physical immobilization and abrupt weight loss (Nash et al., 1991). Due to the limited voluntary use of upper extremity muscles and diminished physical work capacity in persons with quadriplegia, ACE as a potential exercise modality unfortunately does not provide a sufficient exercise intensity to promote cardiac pressure or volume loading (ibid.). However FES-LCE, three times per week for six months results in significant changes in cardiac morphology. Nash et al., (1991) showed an average 6.5% increase in the left ventricular internal dimension at end diastole, 17.5% increase in the septal thickness, 20.3% increase in the posterior wall thickness and 35% increase in the left ventricular mass.

Improved circulation & increased cardiopulmonary fitness. Central and peripheral redistribution of blood is disturbed in people with SCI due to noneffective vasoregulation below the spinal cord lesion. This is caused by the lack of sympathetic vasoconstriction and the inactivated musculoskeletal pump in the legs (Hopman, Verheijen, & Binkhorst, 1993). FES offers a potential solution to the problem of small muscle mass availability and inactivity of the venous pump (Glaser, 1994), by activating the muscle pump below the level of lesion and increasing venous return from the body to the right atrium (Figoni et al., 1991). This, in turn, improves stroke volume, cardiac output, oxygen consumption and reduces myocardial atrophy (Andrews & Wheeler, 1995; Faghri et al., 1992). In one case, acute physiological responses of 30 subjects with SCI performing 30 minutes of FES-LCE increased their mean VO_2 by 225%, decreased their total peripheral resistance by 43% and increased their cardiac output by 69%, from rest to peak levels of FES-LCE (Figoni et al., 1990). Also, in another study, Figoni et al (1991) found that FES knee extension exercise using five to 15 kg on each leg increased rate pressure product by 23 %, increased heart rate by 11% and increased VO_2 by 130% in 14 subjects with C6-T12 lesions (Figoni et al., 1991). The increase in cardiac output was caused solely by an increase in heart rate.

Enhanced rehabilitation. Other peripheral mechanisms, besides the previously mentioned activated muscle pump in the legs, include increased mitochondrial content and oxidative metabolic capacity in paralyzed muscle, improved vascularization and blood flow, and increased neuromuscular adaptation to the stimuli (Krauss et al., 1993).

FES-LCE as a rehabilitation tool can reduce many complications associated with SCI. In one case, a two year FES-LCE program reduced the incidence of pressure sores by 90% and kidney and bladder infections by 50% (Petrofsky, Brown, & Cerrel-Bazo, 1992). Another study, in which individuals with SCI performed six weeks of FES-LCE and 6 weeks of HE exercise, 50% of subjects experienced improved spasticity, 100% improved their endurance, 90% improved their self-image, 90% improved their breathing, and 30% reduced swelling (Hamilton, Krauss, Price, Robergs, & Ruby, 1995). More importantly, FES-LCE has been shown to increase HDL levels by 6% in people with SCI after 4-5 months of training, which would be expected to decrease risk of coronary heart disease (Brenes et al., 1989). Other physical benefits were increased muscle tone, energy, alertness, and cardiovascular fitness (Hamilton et al., 1995).

Increased catecholamine levels in people with SCI. Spinal trauma disrupts the SNS activity below lesion levels and, can alter catecholamine responses (Frey, McCubbin, Dunn, & Mazzeo, 1997). Catecholamine function affects heart rate, myocardial contractility, arterial tone, respiration, thermoregulation, lipolysis, glycolysis, and gluconeogenesis (Ragnarsson, 1993). The area of the sixth thoracic spinal cord segment (T6) has been identified as the critical site for sympathetic innervation of the adrenal medulla (Frey et al., 1997) (see Figure 2.7). Individuals with spinal injuries below T6 demonstrate sympathoadrenal activity similar to the noninjured, while those with injuries higher than T6 do not since the sympathetic chain receives all its efferent preganglionic nerve fibres from the lateral horn of the spinal cord between the first thoracic and second lumbar neurological level (Frey et al., 1997; Ragnarsson, 1993).

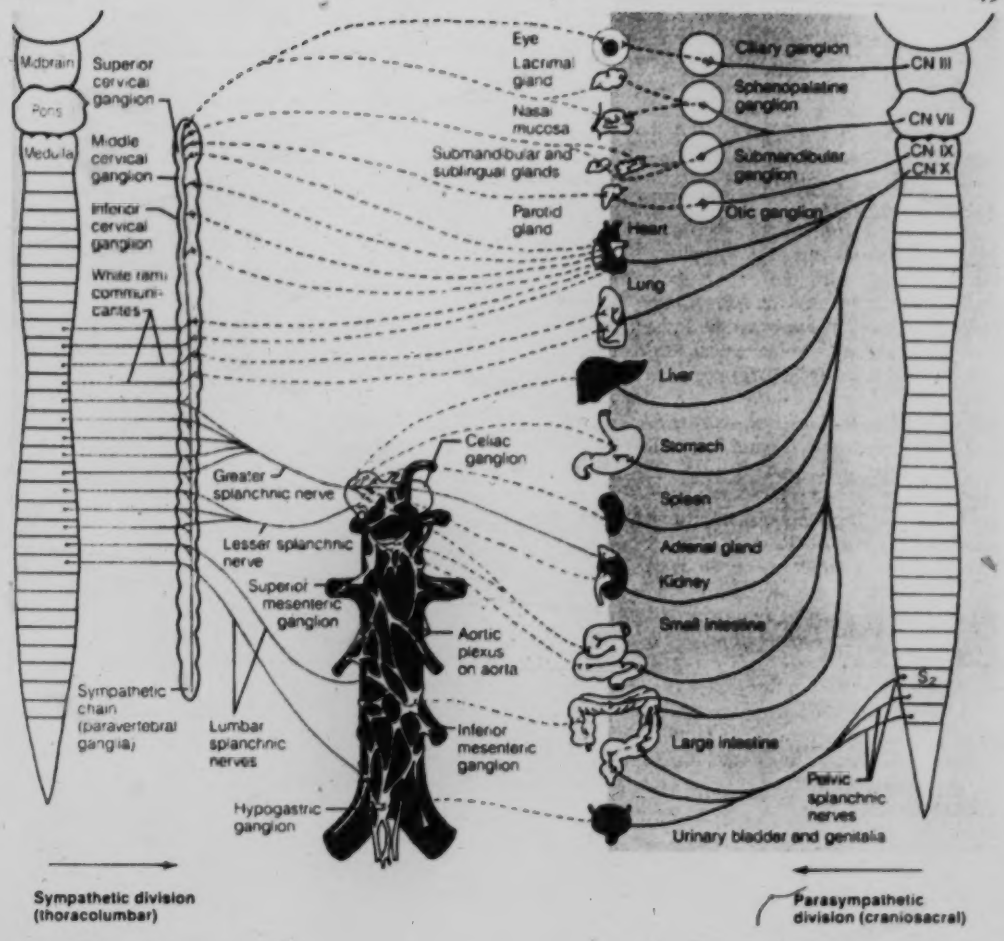


Figure 2.7. Overview of the autonomic nervous system, sympathetic and parasympathetic divisions, issuing from the brain and spinal cord. Solid lines indicate preganglionic axons, while broken dotted lines indicate postganglionic axons. (Although there are four sympathetic lumbar splanchnic nerves, only two are illustrated for simplicity.) Note: CN = cranial nerve. From "The Autonomic Nervous System and Visceral Sensory Neurons," in E.N. Marieb and J. Mallat (Eds.), 1992, Human Anatomy, p. 395. Copyright 1992. Reprinted with permission from the Benjamin/Cummings Publishing Company, Inc.

Research has provided strong evidence for causal relationship between the catecholamine responses to maximal exercise, thus confirming the importance of catecholamines on glycogenolysis (Frey et al., 1997). This relationship was initially investigated by Bloomfield and colleagues (1994). Seven subjects with SCI performed an acute 30 minute bout of FES-LCE and six months of FES-LCE training to investigate the respective roles of afferent feedback and central command in regulating sympathoadrenal response to exercise in people with SCI. After one 30 minute bout of FES-LCE, plasma NE increases ranged between 55-844% and between 35-350% for EP, relative to pre-exercise resting values (Bloomfield et al., 1994). After training for six months with FES-LCE, resting NE decreased by 37% and resting EP decreased by 80% in people with paraplegia. Study findings also revealed that contractions induced by electrical stimulation in <T6 subjects without an intact CNS-spinal circuitry elicited increases in plasma catecholamines, but they were substantially less than 5-to-10 fold increases in the able-bodied population (ibid.).

This relationship was also investigated in a group of people with SCI (four people with lesions above T6 (>T6) and four people with lesions below T6 (<T6)) (Frey et al., 1997). Subjects were to perform a continuous, incremental, peak oxygen consumption test on an arm ergometer. Results showed that the <T6 group exhibited a curvilinear plasma NE and EP response similar to that observed in the able-bodied. According to Burant et al. (1984) who investigated catecholamine response in denervated rat muscle, this increase in catecholamine levels would result in tissue glycogen depletion as his finding showed that denervated muscle had identical sensitivity and response of glycogenolysis to EP in enervated and denervated muscles (Burant et al., 1984). However the >T6 group was unable to increase NE or EP concentrations with increasing workloads and that end-exercise levels did not differ from resting values, thus indicating no increase in sympathetic nervous activity to the adrenals (Frey et al., 1997) . This suggests that there would probably not be a glycogen depletion in people with high lesions.

The absence of glycogen depletion is supported by blood lactate levels, often used as an indicator for muscle glycogenolysis, that were examined by Frey and colleagues (1997). Results showed that blood lactate levels increased as a function of exercise

intensity in both groups, but values were lower in >T6 compared to <T6. As there was no EP response throughout exercise in the >T6 group, it is possible that the maintenance of sympathoadrenal tone in people with quadriplegia is attributed to a local spinal reflex mechanism that operates independently of supraspinal controls (Frey et al., 1997).

Therefore to summarize this topic on catecholamines, it seems that the two studies mentioned above suggest that people with quadriplegia (>T6) have depressed or no catecholamine responses to FES-LCE exercise and that glucose production and lipolysis are impaired (Kjær et al., 1996). This is logical as people with spinal cord lesions above T6 have no sympathetic innervation to the adrenal medulla (Frey et al., 1997). However, it is unclear whether people with paraplegia (<T6) who have similar, however depressed, catecholamine responses during exercise to people without SCI (Bloomfield et al., 1994; Frey et al., 1997), will have a normal relationship between catecholamines, insulin, and lipolysis. Research performed on denervated muscle shows that increasing concentrations of EP resulted in progressive depletion of tissue glycogen (Burant et al., 1984). Furthermore, the sensitivity and glycogenolysis to EP appeared identical in control and denervated muscles (Burant et al., 1984). Hence, it is probable that people with paraplegia and not those with quadriplegia will experience an increase in catecholamines, a decrease in insulin, and increased lipolysis even though the SNS is not intact. This was investigated in the following section.

Lipid and glucose mobilization in SNS versus catecholamines. Karlsson (1997) states that increased fat mass results in increased lipolysis at rest. In turn, it is the concomitant increase in FFA that causes insulin resistance (Karlsson, 1997). However, exercise with FES-LCE can help remedy this problem. When people with SCI exercise with FES-LCE, paralyzed denervated limbs are stimulated to contract, energy consumption increases, and thus glucose uptake increases (Kjær et al., 1996). As exercise persists, energy substrates begin to decrease (Kjær et al., 1996). This relationship was investigated in one study that examined the importance of blood-borne versus neural mechanisms for humoral responses and substrate mobilization during exercise (Kjær et al., 1996). Six males with quadriplegia (C5-T1) aged 24-55 years, performed FES-LCE to

fatigue for 24.6 ± 2.3 minutes. These six males also performed voluntary ACE at a work rate similar to that obtained during involuntary leg stimulation experiments. Six matched long term immobilized males served as experimental controls. Controls performed two bouts of voluntary cycling separated by 90 min of bed rest, on the same apparatus and same body position as those with SCI. Results showed that plasma insulin and NE increased with FES-LCE, however NE remained lower than resting levels in healthy control subjects. EP concentration did not change. Glucose uptake increased with FES-LCE, but glucose production did not change. This was the case even though plasma concentration of lactate increased markedly. In contrast, exercise performed at comparable VO_2 in control experiments increased glucose uptake and glucose production. Mobilization of fatty acids was also diminished during FES-LCE as judged by attenuated increase in plasma glycerol, FFA and β-hydroxybutyrate concentrations. Authors concluded that an intact nervous system, activity in motor centres, and activity in afferent nerves were essential for a normal relationship between growth hormone, catecholamines, insulin, glucose production, and lipolysis. Study findings also suggested that it is the SNS and not EP that is responsible for reducing insulin secretion in exercise. Therefore, compatible with the physiological inverse relationship between substrate mobilization and plasma insulin levels with exercise, the increase in arterial insulin concentration in people with quadriplegia is accompanied by impaired glucose production and lipolysis (Kjær et al., 1996).

Benefits of Hybrid Exercise (HE).

HE exercise has additional benefits when compared to common FES-exercise modalities. The rationale for combining voluntary arm and FES-LCE has been proposed by Hooker et al. (1992). They state that HE 1) activates as much muscle mass as possible, 2) augments autonomic sympathetic outflow to induce appropriate cardiopulmonary responses, 3) reduces lower limb pooling to improve venous return to the heart and cardiac output, 4) creates a higher cardiac volume load to promote central cardiovascular training benefits, 5) enables training at a higher oxygen consumption, and 6) provides training benefits for upper- and lower-body musculature. Subjects with SCI who perform

arm ergometry exercise with FES have been found to have a 28% decrease in blood flow in their legs between no stimulation and high stimulation. This would indicate less pooling in the extremities and more venous return to the working heart (Phillips, Burkett, Munro, Davis, & Pomeroy, 1995). Also, subjects were found to have a decreased rate pressure product which indicates a more efficient myocardial oxygen uptake and an improvement in the efficiency of the cardiorespiratory system when using FES (Phillips et al., 1995).

HE exercise provides superior cardiopulmonary training than either ACE or FES-LCE (Hooker et al., 1992). This superior effect has been attributed to a larger activated muscle mass (Hooker et al., 1992, Glaser, 1994), a greater magnitude of metabolic and cardiopulmonary responses from increased cardiac output and a better circulation of blood to both upper and lower body muscles due to enhanced venous return (Glaser, 1994). This is supported by a study which required eight subjects to complete one exercise test session which consisted of five minutes of seated rest, 10 minutes upright ACE, 10 min seated rest, one minute passive FES-LCE, one minute FES-LCE at 0W, one minute FES-LCE ramping, 10 minutes FES-LCE, 10 minutes of HE exercise, and two minutes cooldown (Hooker et al., 1992).

Results indicated that greater increases in oxygen consumption (VO_2) and cardiac volume load occurred in people with SCI performing HE than in those performing either ACE or FES-LCE alone (Hooker et al., 1992). Stroke volume was not appreciably altered with ACE (reflects venous pooling), but was significantly higher than rest during FES-LCE alone and HE. In addition, VO_2, minute pulmonary ventilation (V_E), HR, total peripheral resistance and arterial-venous O_2 difference responses during FES-LCE alone and ACE were unchanged. However, VO_2, V_E and HR were significantly higher and total peripheral resistance significantly lower during HE than both FES-LCE and ACE performed separately. HE did not significantly alter arterial-venous O_2 difference, but resulted in significantly higher cardiac output than either FES-LCE or ACE performed individually. Therefore HE exercise elicited an increased blood flow and oxygen delivery to active muscle to support the elevated aerobic metabolism (Hooker et al., 1992).

Krauss and colleagues (1993) also reported similar improvements in metabolic and cardiopulmonary responses. In a study conducted by Krauss et al. (1993), eight adult volunteers (aged 23-41 years) with SCI (C5-8/T1) resulting in paraplegia and low level quadriplegia were recruited to perform six weeks of FES-LCE training three times per week for 30 minutes, followed by another six weeks of HE exercise. Individuals were tested maximally on the HE, FES-LCE and ACE before and after the FES-LCE training and the HE training. Results showed that after six weeks of FES-LCE, peak HE VO_2 was greater than peak FES-LCE VO_2, yet smaller than ACE (Krauss et al., 1993). However, after six weeks of HE training, HE VO_2 was greater than both peak FES LE and ACE VO_2 and occurred at a lower heart rate than ACE. It therefore appears that HE exercise may provide more advantageous central cardiovascular training effects than either ACE or FES-LCE alone (Figoni et al., 1990).

FES-LCE or HE exercise.

Literature suggests that HE exercise enhances outcomes observed with FES-LCE training (Hooker et al., 1992; Krauss et al., 1993; Phillips et al., 1995). Also, literature indicates that the recommended exercise protocol should be aerobic in nature (Giada et al., 1991), 30 minutes in duration (Haskell, 1994), at 75% or HR max (Stein et al., 1990) or 50-74% of VO_2 max or heart rate reserve, or 12-13 value on the Borg-RPE (ACSM, 1990) to produce an energy expenditure of 500-3500 kcal/week (Paffenbarger et al., 1986). This protocol optimizes health benefits (Haskell, 1994; Paffenbarger et al., 1986) and increases HDL levels (Hooker & Wells, 1989; Stein et al., 1990). Although FES-LCE exercise can offer 30 minutes of exercise, it is unable to satisfy the other parts of the protocol. In contrast, HE exercise offers 30 minutes of exercise for both the upper and lower body, it increases heart rate to 75% of max, VO_2 to 75%, work and overall kcal/week to 200 kcal per session or 600 kcal per week (Mutton et al., 1997) if it is performed three times per week. Therefore, HE exercise is the best way to optimize health benefits and decrease the risk of CVD.

Part 4: Methodology

Dietary Intake Estimation.

With respect to assessment of dietary intake estimation, four general approaches have been used: dietary history, 24-hour recall, food frequency questionnaires and multiple food records. Each has its strengths and weaknesses (Block, 1982). A brief review of each of these methods is provided below.

Dietary History.

Dietary history is a person's typical food intake in which many details about characteristics of foods usually consumed are assessed. 'Dietary history' coined by Burke & Stuart (1938) is best reserved for diet assessment methods that ascertain a person's usual food intake (Thompson & Byers, 1994). These methods assess details about characteristics of foods usually consumed in addition to frequency and amount of food intake (ibid.). Burke & Stuart's dietary history included three elements: a detailed interview, a food list for amount and frequency, and a three day dietary record (ibid., 1994). Their method, subsequently modified and used in many studies, is an attempt to elicit a usual intake pattern (ibid.).

The major strength of a dietary history is that it assesses usual meal patterns and details of food intake rather than intakes over a short period of time (Thompson & Byers, 1994). On the other hand, it requires an extensive interview by a trained nutritionist (Block, 1982) and also requires respondents to make subjective judgements on usual foods and the amounts eaten which may be difficult for some people (Thompson & Byers, 1994). Another weakness is that it is not useful for individuals who have no particular eating pattern and may be of limited use for individuals who graze (ibid.).

24-Hour Dietary Recall.

A 24-hour dietary recall entails a respondent to remember and report all the foods and beverages consumed in the preceding 24 hours or proceeding day (Block, 1982; Thompson & Byers, 1994). Well trained interviewers are essential for asking probing

questions to gather all information, however it can be administered by persons with less training in a shorter time than dietary history (Block, 1982). Ideally, dietitians educated in food and nutrition are best suited to be interviewers as they are aware of preparation practices, the market place and the regional or ethnic foods (Thompson & Byers, 1994).

Strengths of using the 24-hour recall are: a) the ability of respondent's to recall most of dietary intake; b) time, for the recall requires only 20 minutes which allows less potential for the assessment method to interfere with dietary habits; and c) less potential for the assessment period to interfere with dietary behaviour (Thompson & Byers, 1994). On the other hand, individual diets vary greatly from day to day so that a single day's intake may not be representative. Therefore the 24-hour dietary recall has been criticized for (a) its lack of inter-day variability in individual diets, and (b) its inability to appropriately characterize an individuals usual diet (ibid.). Another reported weakness is that this method relies on the memory of respondents so that if memory is affected, the assessment is not valid (ibid.). One final weakness is that it is costly to hire qualified interviewers which makes this method less accessible for low budget research.

To achieve greater representativeness of usual dietary intake, the seven day recall was developed. However, memories of intake fade rather quickly beyond the most recent day or two so that loss in accuracy can at times exceed representativeness (Block, 1982).

Food Frequency Questionnaires.

Food frequency questionnaires (FFQ) in which respondents report their usual frequency of consumption of each food from a list of foods (Bonifacj, Gerber, & Daures, 1997; Thompson & Byers, 1994) during the past day, week, month or year are increasingly used to measure dietary intake in epidemiological studies (Young & Nestle, 1995). FFQ are most useful for ranking individuals according to food and nutrient intake rather than for quantifying actual amounts of food consumed, since respondents are not asked to state the amount of food they eat (ibid). Some FFQ also incorporate portion size questions, but they are not as accurate compared to dietary records or recalls because longer questionnaires tend to overestimate and shorter ones tend to underestimate dietary intake (Bergman, Boyungs, & Erickson, 1990; Thompson & Byers, 1994).

Strengths of using this method are that it is designed to estimate respondent's usual intake of foods and can be used to circumvent recent changes in diet (Thompson & Byers, 1994). Some food frequency instruments can be self-administered and require little time to complete. Another strength is that respondent burden and data collection and processing are typically much lower that multiple diet records or recall so that FFQ have become a common way to estimate usual diet intake. One particular weakness previously mentioned is that many details of dietary intake are not measured, making it less accurate than dietary recalls and records. FFQ are much better suited for ranking subjects according to food or nutrient intake than for estimating levels of intake (Thompson & Byers, 1994).

Multiple Day Dietary Food Record.

Dietary Records (DR) are designed to elicit information focussing on current diet (Bonifacj et al., 1997). Theoretically, the reporting is done at the time of the eating occasion, but it need not be done on paper. Dictaphones and the Portable Electronic Tape Recorded Automatic system (PETRA) first described by Bingham (1987) have been used and hold promise for low literacy groups (Bonifacj et al., 1997; Thompson & Byers, 1994). DRs differ by the amount of days (d) used (1d, 3d, 4d, 5d, 7d, 9d, and 11d) and also by the technique for measurement (eg. weighing, measuring, estimating). To estimate usual intake of individuals and describe eating patterns or examine the relationship between diet and disease, more than one day dietary information is needed. Eating patterns vary between weekdays and weekends or across sessions, so multiple observations for individuals should include days in all parts of the week and in all sessions of the year. Nonconsecutive days are preferable as they capture more of the variability in an individuals diet (Thompson & Byers, 1994). Typically no more than three or four consecutive days are included, however, it is not decided in the literature whether a 3d DR or 4d DR is better than a 7d DR (Thompson & Byers, 1994). Data shows that each have their downfalls. Three day and four day DRs have been criticized as insufficient to cover the full range of any diet (Bonifacj et al., 1997). Research indicates that there is a significant increase in incomplete records as more days of records are kept,

and the validity of the collected information decreases in the later days of a 7d DR in contrast to collected information in the earlier days (Gersovitz, Madden & Smiciklas-Wright, 1978; Thompson & Byers, 1994). One study attempted to answer the questions by investigating the minimum records necessary for monitoring lipid and caloric intake (Jackson et al., 1986). Results showed that 7, 9, and 11 day records were considered the minimum requirement for a 95% confidence limit, but that 4 consecutive days deemed acceptable as a reasonable compromise for minimal, reliable monitoring of diet compliance.

The particular strength of dietary intake records is its potential for providing quantitatively accurate information on food consumed during the recording period (Thompson & Byers, 1994). For this reason, food records are the "gold standard" against which other dietary assessment methods are compared. One weakness in using this method is that respondent's or respondent proxies must be trained for detail level needed to describe adequately the foods and amounts consumed, including the brand name of the food, preparation methods, recipes for food mixtures and portion sizes (ibid.). This process can be enhanced by contact and review of the report after one day of recording. Another weakness is the demanding task of recording food intake requires motivation and literacy (Block, 1982) which may not be found in low socioeconomic status, recent immigrants, children and some elderly (Thompson & Byers, 1994). As a result many respondents may change their dietary habits or develop the practice of filling out the record at one time for a previous period (ibid.). Responding once every 24 hours is the DR weakness as it makes the record approach the 24-hour recall in terms of relying on memory rather than concurrent recording.

Combining Dietary Resources.

Due to the fact that each method has its strengths and weakness, many investigators combine dietary evaluation methods for their research. Cross sectional surveys which look at dietary habits at one point in time tend to use 24-hour recall, dietary records and FFQ. Case control (retrospective) studies which look at a disease status and try to relate it to the past often use FFQ and dietary history. Cohort

(prospective) studies which compare baseline values and outcomes tend to use multiple dietary recall and records, dietary history, and FFQ. Intervention studies which tend to investigate the effect of an intervention on diet tend to use 24-hour recalls (Thompson & Byers, 1994). However, every investigation has its unique population to consider before deciding on the most appropriate methods.

People with SCI tend to have no particular eating patterns and tend to often eat in restaurants. Recording information is often a problem for people with quadriplegia as some may have decreased writing ability. Recalls are often ineffective as some people do not eat anything in one day and may binge the next. Dietary history and FFQ tend to measure usual intake instead of current intake. For these reasons, dietary records that include the minimum amount of days are the best option for people with SCI, as they are not too time consuming and can give a better representation of a person's current intake.

CHAPTER 3
METHODS & PROCEDURES

Recruitment

Volunteer subjects were recruited from the Edmonton community via advertisements distributed through the Rick Hansen Centre, the Rick Hansen Centre Spinal Cord Injury Treatment Centre Society (SCITCS) FES Clinic, The Canadian Paraplegic Association, and the Edmonton Journal.

Subjects

Eight subjects (seven males, one female) aged 42.5 years (range: 30-53 years), lesions levels between C5 and T8, and injured 18.5 years (range: 3-40 years) were recruited for this study (Table 3.1). The average body mass index was 28.3 kg/m^2. Six of the eight subjects were non-smokers, with one periodic smoker and one smoker. Subjects drank an average of 5.3 ounces a week (Median: 7 ounces/week). Two subjects were non drinkers. All subjects were employed and sedentary. However, one female used a wheelchair for transportation to and from work (1 km) and also performed some weight training on her upper body to prevent injury. This did not change throughout the study.

Subjects were given information on the study (see Appendix B) and asked to complete a form of informed consent (see Appendix C). Following Therapeutic Technologies INC. (manufacturer of ERGYS II) and the ACSM (1990) guidelines for FES-LCE training, subjects underwent general physical examination by a physician at the Rick Hansen Centre. This examination included a medical history, chest and heart examinations, and an examination of body limbs for signs of pressure sores, excessive spasticity, or deformities. In addition, a FES exercise trial was performed to check for simultaneous bradycardia and hypertension termed "autonomic dysreflexia" and the feasibility of using FES to elicit leg muscle contractions required for exercise.

Table 3.1

Subject Characteristics

Sub#	M/F	LOL	BP	Age	TSI yrs	Ht cm	Wt kg	BMI kg/m^2	Drink ou/wk	SM #/mo
1	M	C5	95/50	31	8	165.0	56.1	20.6	12	148
2	M	C5/6	100/80	30	14	174.5	75.0	24.6	7	N
3	M	C5/6/7	87/68	40	3	188.5	113.7	32.0	4	N
4	M	T6	124/77	53	40	156.0	74.2	30.5	5	7.5
5	M	T4	134/84	50	30	162.6	77.9	29.4	7	N
6	M	T5	111/62	44	25	182.4	98.0	29.5	0	N
7	M	C6/7	107/64	42	10	187.5	115.0	32.7	7	N
8	F	T8	110/70	50	18	166.0	76.1	27.6	0	N

Note: Sub # =Subject number, M/F=Gender, LOL=level of lesion, BP=blood pressure, TSI=time since injury, Ht=height, Wt=weight, BMI=body mass index, SM=smoker (cigarettes/month).

Study Overview (see Appendix D)

Prior to beginning the study, participants were weighed and required to complete: a) a consent form; b) a medical exam; c) a three-day food record (see Appendix E); and d) two blood tests separated by five days to control for within person (sample) variability. Diurnal variability was avoided as blood samples were taken in the morning after an overnight 12 hour fast. Blood samples were taken to the University of Alberta Hospital, analyzed for HDL, LDL, TG and TC, batched and frozen at -70 degrees Celsius to be analyzed for HDL_2 and HDL_3 at a later time.

Procedures (see Appendix D)

Following preliminary procedures, subjects were required to complete:

1. Pre-exercise blood test and weight assessment
2. Twenty four sessions of functional electrical stimulation (FES)-leg cycle ergometry training (FES-T) over eight weeks, three sessions per week, 30 minutes per session
3. 24-Hour post-exercise blood test and weight assessment
4. One week of rest (R_1) and three day dietary record
5. Pre-exercise blood test
6. Maximal FES test
7. Four consecutive days of acute FES-leg cycling exercise (FES-A), 1 session per day, 30 minutes per session at 75% exercise intensity
8. 24-Hour post-exercise blood test and weight assessment
9. One week of rest (R_2)
10. Pre-exercise blood test
11. Maximal ACE test
12. Four consecutive days of acute arm crank ergometer exercise (ACE-A), 1 session per day, 30 minutes per session at 75% exercise intensity
13. 24-Hour post-exercise blood test and weight assessment
14. One week of rest (R_3)
15. Pre-exercise blood test
16. Maximal HE test
17. Four consecutive days of acute Hybrid ergometer exercise (HE-A), 1 session per day, 30 minutes per session at 75% exercise intensity
18. 24-Hour post-exercise blood test
19. One week of rest (R_4) with three day diet record.
20. Post-rest blood sample and weight assessment

Blood samples were taken prior to and after each exercise treatment to determine whether blood lipids would return to baseline following one week of rest. Weight was assessed in order to determine whether exercise treatments would alter baseline weight. Dietary records were distributed to subjects in order to determine whether dietary habits would change over the 17 week study. Two dietary records in addition to the initial record at baseline were considered adequate for providing information about subject dietary habits (Harber, 1997) and resulting lipid-lipoprotein profile. The maximal tests provided maximal oxygen consumption with corresponding work load which proved useful for monitoring intensity of exercise training in each of the exercise treatments. FES-T was included in the study as way to train sedentary individuals to perform 30 minutes of FES exercise for four consecutive sessions (FES-A). Without this training, subjects would have been unable to complete the duration of exercise and perform consecutive sessions.

Methods

Three-Day Dietary Food Record.

A three-day dietary food record was completed by the participants to determine whether participation in exercise changed energy intake of fats, carbohydrates and protein see Appendix E). This type of dietary analysis was useful for estimating usual intake of food and describing eating patterns (Thompson& Byers, 1994). This dietary assessment method was chosen since it is the "gold standard" against which other dietary assessment methods are compared (Thompson& Byers, 1994). Its particular strength is its potential for providing accurate information on food consumed during the recording period. However, weaknesses are observed when respondents record only once per day (Thompson& Byers, 1994).

Since one dietary record is often insufficient to determine eating patterns between weekdays and weekends (Thompson& Byers, 1994), three observations were taken prior to eight weeks FES-T, after eight weeks of FES-T, and after HE-A and included two weekdays and one weekend day.

Subjects were required to record food intake immediately following consumption to minimize potential for error in recording. Prior to distribution, the researcher explained how these dietary records were to be completed. Subjects were to fill in the applicable sections which included: individual food/menu items, several ingredients as part of a recipe and toppings or additives, the units of measurement, the number of units, the brand, type, flavour, and method of cooking. For example: bread, slice, 1, Oroweat, 100 % whole-wheat, toasted. Subjects were encouraged not to alter their diets during the study (see Appendix E).

Blood Sampling Procedure.

Blood samples were drawn by an experienced lab technician from the Red Cross Institute. Blood was drawn from the antecubital vein of an extended arm by a sterile 22G x 1 Vacutainer Brand Multiple Sample Needle. Subjects were in a seated wheelchair position. This seating position was optimal for this study due to the logistics of transferring the subjects in a small laboratory setting. The tourniquet was placed around the arm and was released half way through blood collection since prolonged application of the tourniquet during venipuncture can increase apparent lipid concentrations (Henry, 1991). Approximately 4 ml of blood were collected in Becton Dickinson Vacutainer Systems yellow top SST Gel and Clot Activator tubes. A small fraction of this blood was used to fill heparinized micro-hematocrit capillary tubes. Blood samples were cooled at room temperature for approximately 30 minutes until clotted and centrifuged at 5,000 rpm and 4 degrees Celsius for 10 minutes. Serum was drawn from yellow top vacutainer tubes and pipetted into flat top microcentrifuge tubes. The microcentrifuge tubes containing serum were then taken to the University hospital and stored at -70 degrees Celsius. Hematocrits were spun for approximately six minutes, analyzed in duplicate and disposed.

Lipid Analysis.

Subjects were required to perform an overnight fast of least 12 hours. Blood samples were collected for TC, TG, LDL, HDL and HDL subfractions analyses.

Cholesterol was measured using cholesterol esterase. TG was measured using glycerol blanked lipase hydrolysis. HDL was determined directly and enzymatically with the Hitachi 917 Automated Analyser by the addition of cholesterol oxidase coupled with PEG (polyethylene glycol) to amino acids. HDL subclasses were quantified by a dual-precipitation method using dextran sulphate and $MgCl_2$ (Warnick, Mayfield, Benderson, Chen, & Albers, 1982). The first step was to measure HDL through mixing 0.5 ml of serum with 0.05 ml of HDL precipitate solution (dextran sulfate and $MgCl_2$ dissolved in water). This was left to sit for ten minutes before centrifuging at 5000 rpm for 30 minutes on the Hermle Z 233. HDL supernatant was pipetted off and analyzed for HDL on the Hitachi 911. HDL_3 was measured through mixing 0.25 ml of HDL with 0.025 ml of HDL_3 precipitate solution (dextran sulfate and $MgCl_2$ dissolved in water). The sample was let to sit for 10 minutes before it was centrifuged at 5000 rpm on the Hermle Z 233 for 30 minutes. The supernatant was pipetted off and analyzed for HDL on the Hitachi 911. HDL_2 was calculated by subtracting HDL_3 from HDL. LDL concentrations were calculated by the Friedwald equation: LDL cholesterol=TC- [HDL + (TG/5)] (Brown, 1992).

Blood Sample Storage.

All blood samples were analyzed at the hospital by qualified technicians. This was arranged prior to collection between the researcher and the laboratory contact person in charge of research and special projects. Initially, samples were collected and immediately analyzed. Once analyzed, these samples were stored for future HDL subfraction analyses. This became a problem as there were few subjects and few blood samples. Because subjects did not begin the study all on one day, individual samples, sometimes just one, were delivered for analysis on different days. This staggered analysis of blood samples may have been one of the reasons why some baseline samples were lost. This was also complicated by the fact that the initial blood sampling was followed by eight weeks of FES-T exercise during which no blood samples were taken. After eight weeks of exercise blood testing began, but subject files were missing and no records could be found. The laboratory contact person explained that samples had been stored in a freezer which had

suddenly been defrosted. Blood samples, mostly baseline and pre-FES-T, disappeared during this process. Without confirmed knowledge of whether there had been lost samples, the researcher continued the study. This time, samples were stored together so that they could be collectively analyzed at a later time. This ensured proper control of the samples and no further complications arose. After the completion of the study, the loss of blood samples was confirmed. These samples included three days of baseline testing, one post-FES-T sample, and two pre-FES-A samples needed for HDL and HDL subfraction analyses, and three pre-FES-A samples for TC and TG analyses. Fortunately, all subjects had at least one sample that could be used as a baseline sample. All other samples were lost and consequently, data analysis was affected. Due to the fact that only one post-FES-T sample was lost, analysis was performed on baseline, post-FES-T, post-FES-A, post-ACE-A, and post-HE-A samples.

Maximal Aerobic Power Determination.

Maximal aerobic power was determined using the Beckman MMC Horizon™ System. The MMC is a respiratory gas analyzer which is housed in a mobile cart. It contains analyzers for O_2 and CO_2 which measure the concentrations of expired gases. It also contains transducers which measure the volume and temperature of expired breath.

The subject breathes into the MMC via a valve which routes inspired air (or gas) to the subject and routes the subject's expired (exhaled) gas into the MMC. The valve is designed to minimize the "dead space" within the valve, thus minimizing the amount of gas rebreathed by the subject. The breath path accepts expired breath from the subject and routes it to the mixing chamber. The three litre mixing chamber mixes the gases from several successive breaths to form an average concentration of mixed expired gases which can be sampled by the analyzers in the sample path. The expired breaths flow through the mixing chamber and out through the turbine and breath switch, and then through the exhaust hose to the atmosphere outside the MMC cabinet.

The mixed expired path samples gas from the mixing chamber and dries the sample in a drier. The sample then flows through a sample select valve (V_2 for mixed expired sample), and through a small particle filter into the analyzers. The CO_2 and O_2

analyzers measure the concentrations of CO_2 and O_2 in the sampled gas. Then the sample flows through the pump, through an indicating flowmeter, and then to the atmosphere or to the mixing chamber (SensorMedics, 1983).

Criteria for maximal aerobic power (VO_2 max).

The criteria for maximal aerobic power was four fold: subjects had to attain a VO_2 plateau where any further increment in resistance or time did not increase VO_2; a respiratory exchange ratio greater than 1.10; HRmax calculated from the following equation: 220 minus subject age plus or minus ten beats per minute; and a Borg-rate of perceived exertion (RPE) scale value of greater than or equal to 17 (see Appendix F).

Maximal FES-Leg Cycle Ergometer (FES-LCE) Test.

Maximal aerobic power was measured using the ERGYS II (Therapeutic Alliance, Inc.) FES-LCE which permitted researchers to adjust resistance manually without pushing the stop button, going into a two minute cool down, resetting the resistance, and starting over. Therefore, based on an individual's ability to maintain revolutions per minute, the researcher would manually adjust resistance.

The Borg- RPE scale was administered every two minutes of the test, and after the completion of each load. RPE-values, heart-rate and resistance were all recorded at this time.

Subjects began with a technician-assisted warm-up for one minute. After warm-up, stimulation increased until the legs could cycle unassisted. In the second minute of cycling the resistance ramped up to a maximum. At this point the resistance could be reduced if it was doubtful that the subject could finish at that level. Subjects were required to perform five minutes of exercise at a set resistance as to allow three minutes of cycling at the desired level. After five minutes of cycling were completed, a two minute technician assisted cool down was completed. Once the cool down was completed, researchers increased the resistance thereafter by 1/8kp (6W) or .5/8 kp (3 W). Subjects were required to continue to pedal until their legs could no longer pedal 35 rpm at a particular load.

Maximal Arm Crank Ergometer (ACE) Test.

For the maximal ACE test, subjects were required to arm crank a modified electronic cycle ergometer while seated in their wheelchairs (Gass, Harvey, & Gass, 1995). People with paraplegia and quadriplegia performed a warm up at 0,25,50 W (Bostom et al., 1991), and 0, 2.5, 5W or 0, 5, and 10 W, respectively for 4 minutes. The arm crank was calibrated so that 5 W equalled approximately 0.2kg. Starting load was estimated during warm-up based on upper body strength, balance and subject Borg-RPE scale. After warm-up, subjects were encouraged to rest for two minutes. Following this rest period, maximal oxygen consumption was determined using a continuous graded arm crank exercise test. Subjects began at 2.5, 5 or 25 W at 50 rpm (Bostom et al., 1991, Krauss et al., 1993; Bloomfield et al., 1994; and Gass et al., 1995) and load was increased 5-10 W for people with paraplegia and by 2.5 -5 W for people with quadriplegia (Bloomfield et al., 1994) every two minutes. The Borg-RPE Scale was administered before the end of each two minute period. Heart rate and load were recorded at this time. Subjects with quadriplegia were able to maintain a voluntary effort with the aid of Velcro-closure gloves which assured a grip on the arm crank. Subjects were instructed to signal the experimenters when he or she was within one minute of exhaustion. The researcher then took the last minute Borg-RPE scale and heart rate recordings to prepare for cool down. Cool down required subjects to exercise at a comfortable cadence for two minutes.

Maximal Hybrid Ergometer (HE) Test.

A maximal HE test was used to measure maximal aerobic power. This test required a subject to voluntarily crank an arm ergometer while pedalling the FES-LCE (Krauss et al., 1993). In this study, the protocol was modified so that resistance was such that it allowed a subject's legs to complete 30 consecutive minutes of exercise without fatigue. The Borg-RPE scale was administered every two minutes throughout the test, and subject scores and heart rate were measured at this time.

Subjects performed a 12 minute warm up with ACE and technician-assisted passive leg pedalling, prior to beginning the test. During testing, resistance increased

every four minutes followed by a two minute rest period. The subject began the first minute of ERGYS II controlled warm-up with technician-assisted leg pedalling while simultaneously cranking the ACE without resistance at a comfortable cadence. After this first minute of exercise on the ERGYS II, stimulation intensity increased so that legs could cycle unassisted and in the second minute the resistance began ramping up to its maximum. Once the subject was comfortable with the exercise on the leg-cycle, the ACE was implemented. The ACE started at 50% of the maximal attained load on the ACE max test (Krauss et al., 1993). Load was increased by 2.5-5 Watts (.1-.2kg), depending again on whether it was a subject with paraplegia or quadriplegia, every two minutes until the subject could no longer increase load or oxygen consumption. Thereafter, the subject maintained ACE watts until he/she could no longer increase load or legs fatigued (cadence less than 35rpm). Once subjects had reached their peak there was a two minute cool down on the bike and on the ACE simultaneously. Subjects were able to modify load so that a comfortable effort was attained. Subjects were permitted to continue their cool down, while they were detached from the apparatus.

Subjects who could not pedal unassisted were provided a technician for the testing procedure.

FES-Training (FES-T).

A protocol developed by Krauss et al. (1993) was used in this study. Subjects in this study completed 24-26 bouts of exercise with ERGYS II in eight weeks. Each training session began with a one minute warm-up assisted by a FES technician to attain 40 rpm. At the end of the one minute warm-up period, the first interval period began and was characterized by a progressive increase in electrical stimulation allowing the subject to pedal unassisted until fatigue (unable to pedal at 35 rpm). Instead of the five minute intervals in Krauss et al. , subjects in this study completed three 10 minute exercise sessions to complete 30 minutes of discontinuous exercise per training session. If the subjects were not able to complete 10 minutes of exercise due to fatigue, assistance was provided to maintain 40 revolutions per minute while keeping 100% of maximum stimulation until the 10 minute period was completed. A technician-assisted cool down

period, where minimal stimulation was provided for two minutes, was implemented after each 10 minute period was finished. Due to the computer program (ERGYS II) used in this study, the cool down period was followed by five minutes of rest instead of three minutes in Krauss et al. Following the rest period, unlike Krauss et al. who implemented another one minute warm-up, subjects began another exercise period with the same training, cool down, and resting procedures until 30 minutes of exercise were completed. If subjects were able to complete ten minutes of exercise without fatigue, subjects continued exercising until they reached the next ten minute interval or completed the exercise.

FES-Acute (FES-A).

After eight weeks of training, individuals were required to complete four 30 minute bouts of FES-LCE in one week. The resistance attained after eight weeks determined the training resistance for the acute bouts of exercise. A training session began with a one minute warm-up assisted by a FES technician to attain 45 rpm. After one minute, progressive electrical stimulation allowed subjects to pedal unassisted at 40 rpm. Subjects were required to pedal unassisted for 30 minutes. If subjects were not able to pedal unassisted for 30 minutes, assistance was provided until 30 minutes of exercise were completed. The session ended with a two minute technician assisted cool down.

ACE-Acute (ACE-A).

Following the FES-A training, subjects performed four consecutive bouts of exercise on the ACE. This exercise was performed at RPE-values of 12-13 (somewhat hard), and 75% of attained work load, heart rate, and maximal oxygen consumption (VO_2) during maximal ACE testing.

The ACE-A training did not have a planned warm-up. Subjects began exercising on the ACE-A and slowly increased training intensity to 75%. Heart rate and RPE-value checks were performed randomly over 30 minutes of exercise, but subjects were responsible for monitoring their heart rate and working intensity. After 30 minutes of exercise, subjects performed 2-5 minutes of cool down.

Hybrid-Acute (HE-A).

Hybrid training includes both upper and lower body training. In this case, subjects performed simultaneous FES-LCE and arm crank ergometry. A HE-A session began with one minute of arm cranking at a comfortable cadence while simultaneously performing FES-LCE technician assisted warm-up. After this first minute maximum stimulation increased and fluctuated so that legs could pedal unassisted for 30 minutes. Once legs could pedal unassisted, load was added to the arm crank ergometer so that subjects were exercising at approximately 75% of peak VO_2. If subjects were not able to pedal unassisted, assistance was provided until 30 minutes of training were completed. The resistance on the FES-LCE began at 0W and increased by 1/8 kp or approximately six Watts if the subject terminated a session without reaching maximal stimulus.

Blood Pressure.

Blood pressure was measured via auscultation: a) five to 10 minutes before exercising; b) every 30 seconds of exercise; c) during the exercise cool down; and (e) at the end of the exercise session if a subject showed any signs of autonomic dysreflexia. Otherwise blood pressure was assessed periodically during the exercise.

Heart Rate.

Heart rate was assessed by a Polar Heart Rate Monitor during maximal tests and throughout ACE-A and HE-A.

Weight.

Weight was measured before and after eight weeks of FES-T, and after FES-A, ACE-A, and HE-A. Subjects transferred onto an adapted scale for weight measurement. The adapted scale was a chair with a metal base which sat on a regular scale and had a medal bar connecting its two legs on which subjects placed their feet.

This method was effective for six of the eight subjects, but was inaccurate for those individuals weighing more than 100kg.

Energy Expenditure.

Energy expenditure was calculated according to VO_2 measured during maximal testing. Heart rate, peak VO_2 value, peak work rate, and RPE-Borg scale were compared to find the most suitable VO_2 at 75% intensity of exercise. Then approximately one minute of VO_2 measurements and corresponding respiratory exchange ratios (RER) were averaged. The average RER value was subsequently used in a table (McArdle, Katch, & Katch, 1991, pp.153) to determine a caloric equivalent per litre of oxygen consumed (McArdle et al., 1991, pp. 802).This equivalent was then multiplied by the average VO_2 in one minute and then multiplied by the number of minutes the exercise was performed. Energy Expenditure (Kcal/min)= VO_2 (litres/min) x caloric equivalent per litre of O_2 at a given steady-rate respiratory quotient (McArdle, et al., 1991, pp. 802).

Power Output (W).

Power output was calculated based on the following formula:

$$\frac{(R \times 9.81)(RPM \times d \times t)}{T}$$

Where R is resistance (kg); 9.81 m/s^2 is gravitational force; RPM is revolutions per minute; d is distance travelled per revolution (5.965 m for ERGYS system and 2.4 m for Monark 881 system); t is time in minutes; T is time in seconds.

Data Collection

The independent variables were the exercise interventions which included FES-T, FES-A, ACE-A, and HE-A. The dependent variables were a) blood fractions: total cholesterol (TC),TG, LDL, HDL, HDL_2 and HDL_3, b) dietary variables, and c) weight. Other variables reported during the study were lesion level, blood pressure, heart rate, VO_2, training resistance, exercising work rate, exercising power output, age, years post-injury (time since injury), height, BMI (kg/m^2), number of cigarettes smoked per month, and number of drinks (ounces) consumed per week.

In the data collection phase, blood samples brought to the University of Alberta Hospital for analysis went missing. It was believed that the -70 degree Celsius

refrigeration unit in which the samples were stored incurred some mechanical problems and was subsequently defrosted. Refrigeration contents were either disposed or transferred to another unit. It was during this process that research blood samples were lost.

Data Analysis

This study followed a reverse design (O1, T1, O2, O3, T2, O4, O5, T3, O6, O7, T4, O8, O9 where O refers to observations and T refers to interventions). The purpose of this design (as with time series) is to determine a baseline measure (O1), evaluate the treatment (O1-O2), return to baseline (O2-O3), evaluate the treatment (O3-O4), return to baseline (O4-O5), evaluate the treatment (O5-O6), and return to baseline (O6-O7) etc.. The advantage of using this design is that it can also be used for single-subject research. Instead of one group, a single subject is followed across all time periods (Thomas & Nelson, 1990). All data were analyzed using the Statistical Package for the Social Sciences (SPSS). A computer software program (Food Processor Plus, Version 6.01) was used to calculate average daily intakes of total energy, grams of fat, carbohydrate and protein.

Lipids, lipoproteins, and three day dietary variables were analyzed at an alpha level of ≤ 0.05 as significant, adjusted by the Bonferroni correction, using repeated measures ANOVA and multiple two-tailed t-tests for paired samples. A repeated measures ANOVA was used to determine differences over time in subjects with quadriplegia and those with paraplegia relative to baseline. Also, repeated measures ANOVA was used again to determine differences in lipid-lipoprotein profile between people with paraplegia and quadriplegia with exercise. Energy expenditure, VO_2 max, heart rate, and RPE-values were statistically compared at an alpha level of ≤ 0.05 as significant, adjusted by the Bonferroni correction, using multiple two tailed t-tests for paired samples. Differences between people with quadriplegia and paraplegia were determined using two-tailed t-test for independent samples using an alpha level of ≤ 0.05 as significant.

Due to the small sample size and the large number of missing samples, a single-subject design was also used for lipid and dietary analysis. Some figures were created to illustrate trends which proved helpful for analysis.

A correlation matrix was constructed for the sample to determine the relationship between variables. Values were considered significant at an alpha level of < 0.05. Due to the number of variables included in the matrix, the figures are not represented in a table. Correlations that were found to be significant are discussed in chapter four.

Missing data were not substituted with computed averages or random values as this may have biased the data due to the small sample size. Missing samples were included in the multiple t-test analyses. As a result of missing cases which were excluded from the analyses, sample numbers were at times reduced to between four and eight. On the other hand, missing cases were avoided in the repeated measures ANOVA by using initial baseline levels and post-exercise levels. This decision was based on the fact that missing samples were found in the pre-exercising or resting samples and that a repeated measures ANOVA on resting levels did not result in any significant findings. In single subject analyses, missing samples were taken into consideration when the data were discussed. Missing samples were represented by a hyphen in the tables at the end of the chapter four.

Ethical considerations

When surveyed about concerns subjects have regarding FES-LCE, responses centered around not having access to the bicycle following termination of the training program. Some individuals expressed concerns over the time consuming nature of training given that a single training session could involve up to one hour of transportation to or from the training site, as well as one to two hours of preparation and actual riding (Hamilton et al, 1995). Subjects were required to attend the training sessions at the Rick Hansen Centre as the equipment was immobile.

Safety.

Autonomic dysreflexia.

Peripheral stimulation below lesion level can induce an exaggerated reaction with a clinical picture of profound hypertension, sweating above lesion level, baroreflex mediated vagally induced bradycardia (fall in heart rate), increase in blood pressure (predominantly systolic), skin and muscle vasoconstriction and pounding headache (Ashley et al., 1993; Karlsson, 1997). This reaction is the so-called autonomic dysreflexia reaction (Karlsson, 1997). The postulated mechanism is as follows (Ashley et al., 1993).

Electrical stimulation is turned on and immediately perceived as a noxious stimulus by intact pain receptors in the paralyzed limbs. Pain receptors relay via C pain fibers to the spinal cord, ascend the spinal cord, and give collateral connections to the preganglionic sympathetic bodies of the intermediolateral horn to result in a mass sympathetic discharge below the level of the lesion (Ashley et al., 1993; Burnham et al., 1994). Peripheral piloerection and vasoconstriction occur, as is clinically manifest by gooseflesh, shivering, and pallor distal to the level of injury, along with systemic hypertension (Ashley et al., 1993; Burnham et al., 1994).The hypertension stimulates aortic and carotid baroreceptors, activating the parasympathetic nervous system proximal to the level of SCI and causing facial flushing, vascular headache, and nasal stuffiness (Burnham et al., 1994). The aortic arch and carotid sinus baroreceptors also relay messages, via the vagus and glossopharyngeal nerves, to the tractus solitarius and vasomotor area in the ventrolateral medulla to result in a two fold response: 1) bradycardia from the vagal centre which is of little use in counterbalancing the hypertension; and 2) vasodilation activity within descending inhibitory fibers (Ashley et al., 1993). However, the fibers are unable to traverse the spinal lesions so that the parasymphathetic effect of the vagus nerve is essentially unopposed by the antagonistic SNS response which results in reflex vasodilation above the lesion and unchecked vasoconstriction and hypertension below the lesion (Ashley et al., 1993; Burnham et al., 1994; Ragnarsson, 1993). Thus a compensatory drop in blood pressure cannot occur and hypertension persists, or is increased, as stimulation is increased (Ashley et al., 1993).

This reaction is controlled through monitoring BP and heart rate, and adjusting the intensity of stimulation. Research shows that after the stimulus is removed, heart rate substantially rebounds and BP returns to normal levels (Ashley et al., 1993). This response is highly reproducible and suggests caution be exercised in the use of FES for people with SCI with lesion levels above T6 (Ashley et al., 1993).

Thermoregulatory dysfunction.

Temperature control is an important consideration when performing ACE or FES-LCE (Petrofsky, 1992). In one study, people with quadriplegia showed a linear increase in core temperature with workload at environmental temperatures of 30 and 35 degrees C (Petrofsky & Phillips, 1984). Work could be tolerated at 30 and 35 degrees C for quadriplegics, but not in a 40 degree C room. The intolerance for exercise was explained with respect to sweat rate. Specific examination of regional sweat rates below the neck in the people with quadriplegia or below the waist in people with paraplegia showed no increases in sweat rates with training. Recommendations indicate that unless special heat exchange clothing is used, subjects with paralysis involving a significant portion of the body should not exercise above 80 degrees F room temperature to any large extent (Petrofsky & Phillips, 1984). People with quadriplegia must be extremely careful with any type of exercise in a non air-conditioned room (Petrofsky & Phillips, 1984). The researcher avoided thermoregulatory problems as the study was undertaken in an airconditioned room.

Bruising.

There is the risk of bruising and tenderness of the skin as a result of venipuncture. The researcher attempted to reduce this risk by using a certified phlebotomist to perform the procedure.

Electrode Burning.

FES electrodes can burn skin. Due to the loss of sensation, a person with SCI may burn and not realize it. The researcher attempted to prevent burning through a)

purchasing spandex shorts with pockets for electrode placement; b) the application of sufficient Liqui-cor (Burdick; Milton, Wisconsin), which is a conductive cream, as to reduce the impedance of the skin; and c) periodically checking the colour of the skin for any signs of burning.

CHAPTER 4

RESULTS

Lipids: Group Analysis

There were no significant findings regarding lipid and lipoprotein levels following FES-T, FES-A, ACE-A, and HE-A exercise. Results are reported in Table 4.1 and 4.2.

Table 4.1

Means and Standard Deviations for all Lipid Variables

Variable	Base	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
Variable	chol1	chol2	chol3	chol4	chol5	chol6	chol7	chol8	chol9
Mean	4.47	4.67	4.92	4.70	4.83	4.81	4.69	4.90	4.79
SD	0.83	1.03	1.18	1.03	1.06	0.87	1.00	1.11	1.06
Variable	hdl1.1	hdl1.2	hdl1.3	hdl1.4	hdl1.5	hdl1.6	hdl1.7	hdl1.8	hdl1.9
Mean	0.99	1.02	1.02	1.00	1.04	1.03	1.01	1.09	1.00
SD	0.32	0.28	0.19	0.22	0.31	0.28	0.29	0.29	0.23
Variable	hdl2.1	hdl2.2	hdl2.3	hdl2.4	hdl2.5	hdl2.6	hdl2.7	hdl2.8	hdl2.9
Mean	0.22	0.23	0.22	0.15	0.21	0.21	0.22	0.28	0.23
SD	0.20	0.20	0.20	0.15	0.21	0.21	0.19	0.21	0.16
Variable	hdl3.1	hdl3.2	hdl3.3	hdl3.4	hdl3.5	hdl3.6	hdl3.7	hdl3.8	hdl3.9
Mean	0.77	0.81	0.87	0.80	0.83	0.73	0.79	0.81	0.77
SD	0.13	0.16	0.01	0.11	0.13	0.29	0.11	0.12	0.09
Variable	ldl1	ldl2	ldl3	ldl4	ldl5	ldl6	ldl7	ldl8	ldl9
Mean	3.11	3.32	3.62	3.40	3.46	3.49	3.39	3.52	3.44
SD	0.64	0.76	1.08	0.87	0.87	0.76	0.84	0.98	0.94
Variable	tg1	tg2	tg3	tg4	tg5	tg6	tg7	tg8	tg9
Mean	1.82	1.34	1.39	1.51	1.62	1.43	1.44	1.44	1.68
SD	0.69	0.47	0.37	0.69	0.84	0.54	0.44	0.61	0.70

Note: 1,2,3,..9 correspond to blood samples. Base = baseline; chol = cholesterol; hdl = high density lipoprotein (HDL); hdl2 and hdl3 = HDL subfraction 2 and 3; ldl = low density lipoprotein (LDL); tc = total cholesterol.

Table 4.2

Means and Standard Deviations of Lipid and Lipoprotein Ratios

Variable	Base	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
Variable	h2/h3.1	h2/h3.2	h2/h3.3	h2/h3.4	h2/h3.5	h2/h3.6	h2/h3.7	h2/h3.8	h2/h3.9
Mean	0.27	0.28	0.26	0.21	0.24	0.36	0.26	0.33	0.29
SD	0.21	0.22	0.22	0.25	0.22	0.33	0.21	0.23	0.18
Variable	hdl/ldl	hdl/ldl	hdl/ldl	hdl/ldl	hdl/ldl	hdl/ldl	hdl/ldl	hdl/ldl	hdl/ldl
Mean	0.32	0.31	0.30	0.30	0.31	0.30	0.31	0.32	0.30
SD	0.08	0.06	0.07	0.08	0.08	0.08	0.08	0.07	0.08
Variable	tc/hdl	tc/hdl2	tc/hdl3	tc/hdl4	tc/hdl5	tc/hdl6	tc/hdl7	tc/hdl8	tc/hdl9
Mean	4.75	4.72	4.87	4.79	4.82	4.84	4.82	4.62	4.87
SD	1.37	0.87	1.13	0.99	1.28	1.14	1.19	0.93	1.21

Note: 1,2,3..9 corresponds to blood samples. Base = baseline; chol = cholesterol; hdl = high density lipoprotein (HDL); hdl2 and hdl3 = HDL subfraction 2 and 3; h2/h3 = HDL_2/HDL_3; ldl = low density lipoprotein (LDL); hdl/ldl = HDL/LDL; tc = total cholesterol.

Of note, no significant (±5%) blood volume changes occurred with exercise. Therefore, no adjustments were made to lipid and lipoprotein values.

Although there were no significant changes in HDL, HDL_2, HDL_3, TG, and TC levels after training, trends became apparent after plotting percent change in lipid-lipoprotein profile with each exercise intervention. However, percent change was only considered significant when there were clinical implications (CVD risk reduction). Figure 4.1 and 4.2 illustrate these trends and demonstrate that HE-A had a greater effect on HDL and its subfractions than FES-T, FES-A and ACE-A. Additionally, all exercise interventions decreased TG levels and increased LDL and TC.

From this point on people with quadriplegia will be referred to as Quads and people with paraplegia will be referred to as Paras.

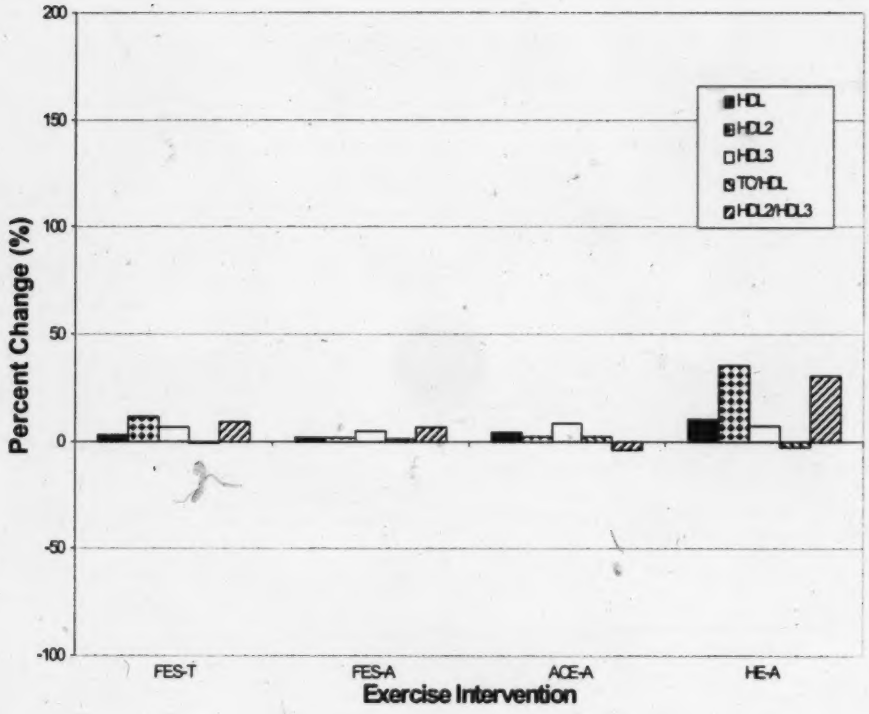


Figure 4.1. Percent change in HDL, HDL_2, HDL_3, TC/HDL, HDL_2/HDL_3 for group (n=8) with FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

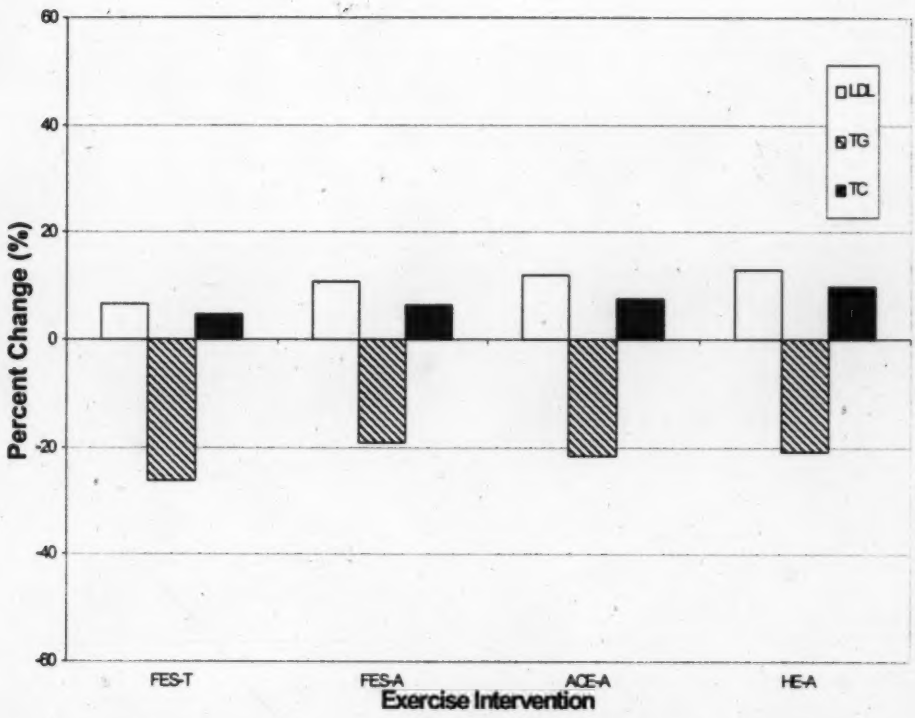


Figure 4.2. Percent change in LDL, TG, and TC for group (n=8) after performing FES-T, FES-A, ACE-A and HE-A relative to baseline levels.

Difference Between Quads and Paras.

After performing a two-tailed t-test for independent samples, no significant differences were found for HDL, HDL_2, HDL_3, LDL, and TG. However, repeated measures on Quads and Paras showed a significant increase in LDL over time in Paras ($p=0.045$, Effect size= 0.53 and Power= 0.673). Below is a descriptive analysis of the group after calculating percent change in an attempt to demonstrate trends.

HDL: Overall, the largest increases in Quads occurred with FES-A (11%) and HE (10%), whereas the largest increases in Paras were with ACE (9%) and HE (10%). The largest difference in HDL levels between Quads and Paras occurred during FES-A, where Quads increased 11% and Paras decreased 7% (see Figure 4.3).

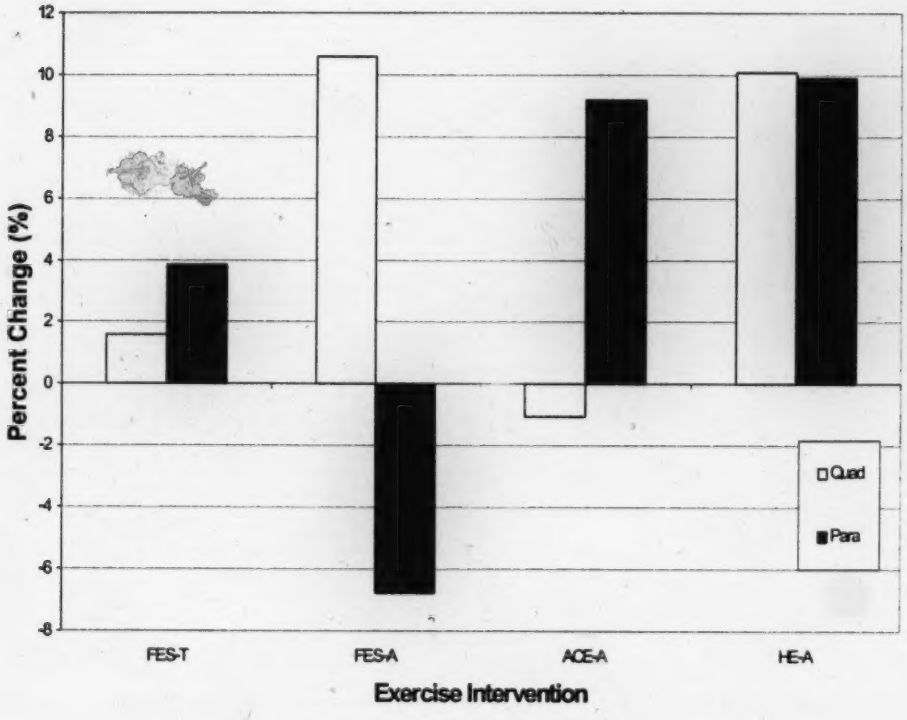


Figure 4.3. Percent change in HDL levels in people with quadriplegia (Quads) versus people with paraplegia (Paras) after performing FES-T, FES-A, ACE-A and HE-A relative to baseline levels.

HDL_2: Quads incurred their largest increases during FES-A (42%) and HE-A (77%)while Paras incurred theirs during FES-T (16%) and HE-A (13%) (see Figure 4.4). In contrast to Quads, HDL_2 levels decreased in Paras after performing FES-A (-19%).

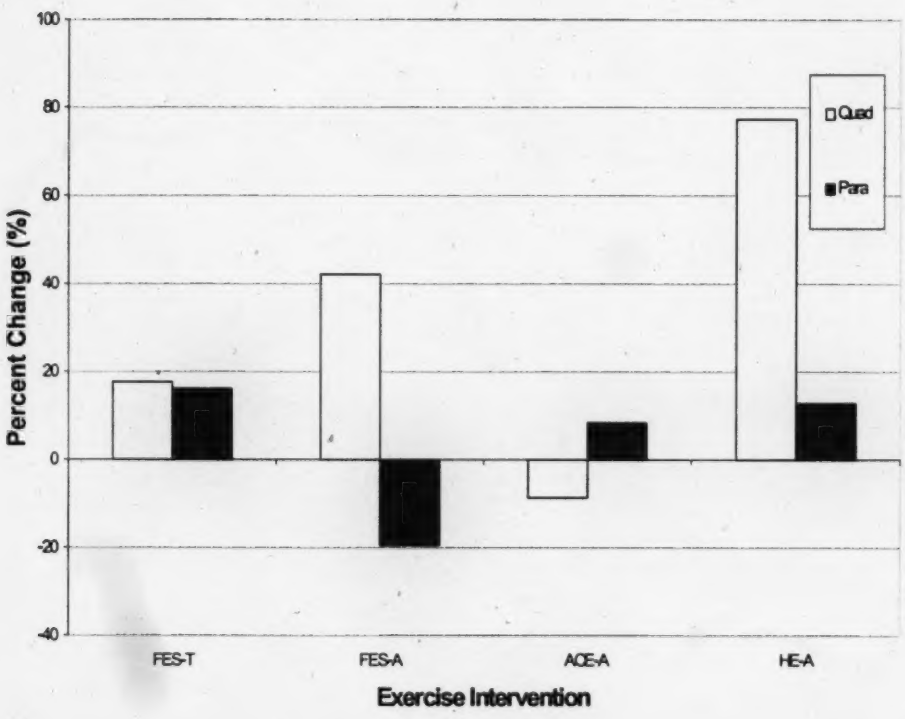


Figure 4.4. Percent change in HDL_2 levels in Quads (n=4) versus Paras (n=4) after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

HDL_3: No changes were observed in Quads except for a slight increase during FES-A (6%). In contrast, HDL_3 levels for Paras increased with FES-T (14%), ACE-A (15%), and HE-A (15%) and decreased (11% from FES-T) with FES-A. The absence of a bar for Quads in HE-A is explained by a 0% increase from baseline after HE-A (see Figure 4.5).

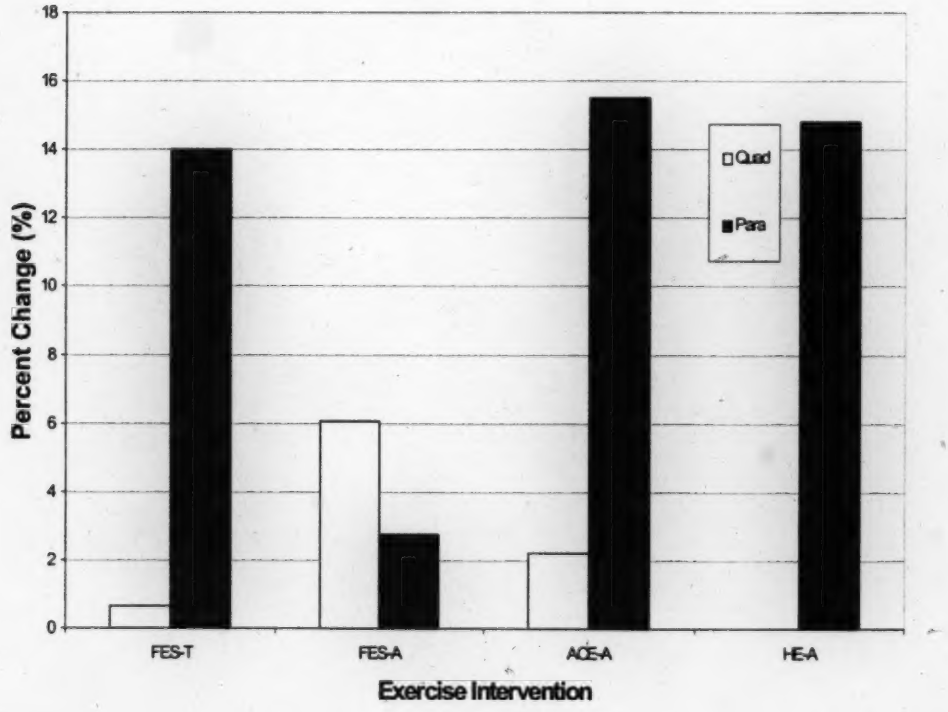


Figure 4.5. Percent change in HDL_3 levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

TC/HDL: This ratio increased slightly (9%) with ACE-A in Quads and (8%) with FES-A in Paras (see Figure 4.6). After completing HE-A the TC/HDL ratio was slightly below baseline levels.

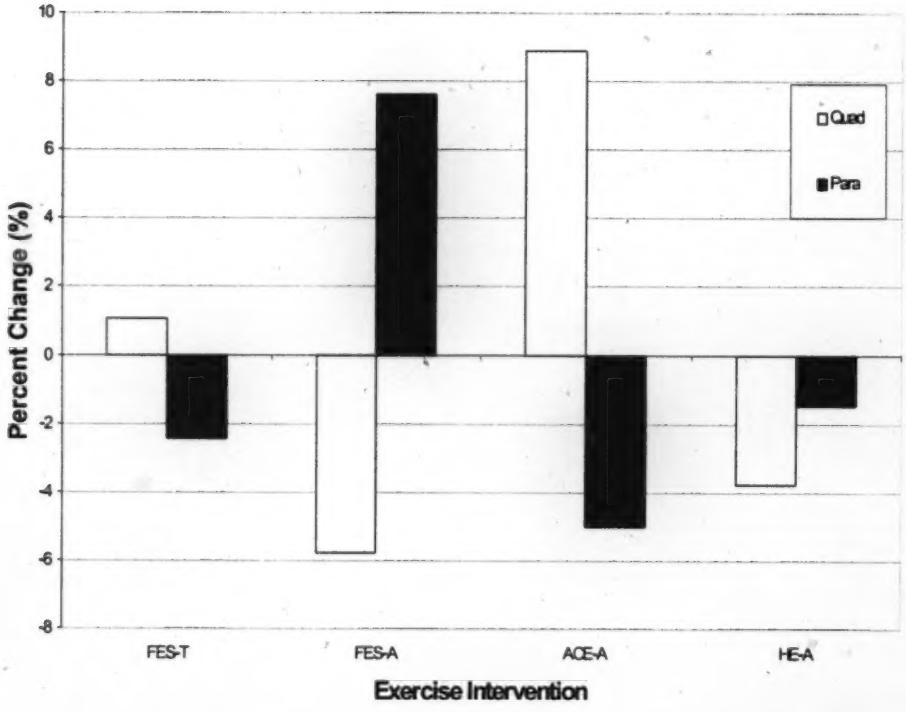


Figure 4.6. Percent change in TC/HDL ratio in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

HDL_2/HDL_3: Overall, Quads increased with FES-T (21%), FES-A (29%) and HE (68%) and decreased with ACE-A (-12%) (see Figure 4.7). In Paras this ratio increased to a lesser extent with FES-T (9%), and HE-A (9%) and decreased (-6%) with FES-A. As shown below (Figure 6), the largest increase occurred in Quads after performing HE-A.

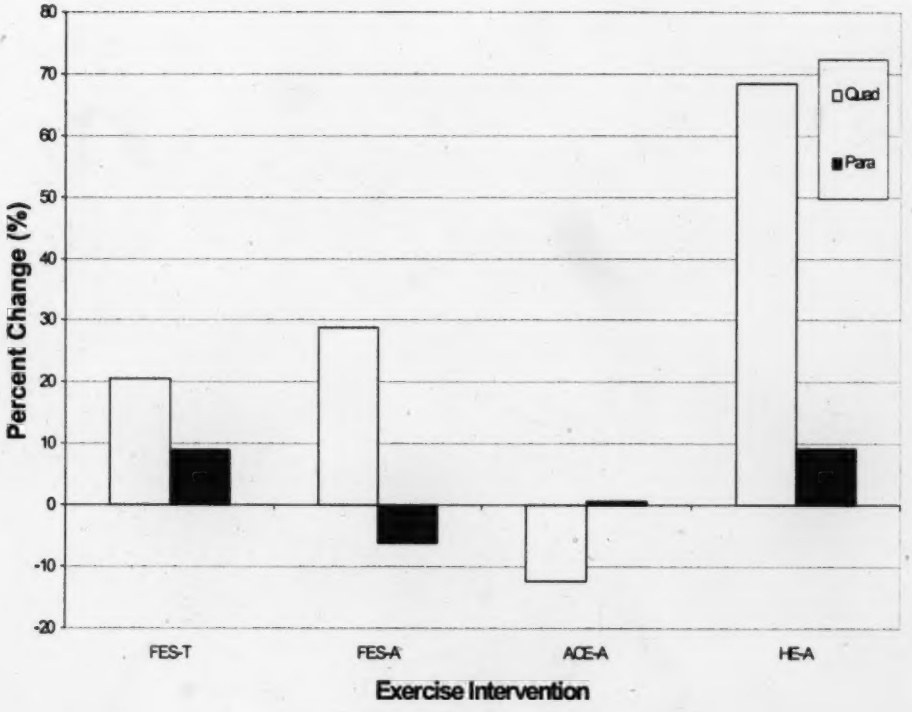


Figure 4.7. Percent change in HDL_2/HDL_3 ratio in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

LDL: No changes were found in Quads (±5%), except for after performing ACE-A (see Figure 4.8). In contrast, LDL levels were significantly elevated in Paras after performing all exercise interventions; FES-T (11%), FES-A (19%), ACE-A (14%), and HE-A (24%). Noteworthy to mention is that LDL levels in Paras and Quads increased to CVD risk levels after R_2 and remained at risk throughout the study.

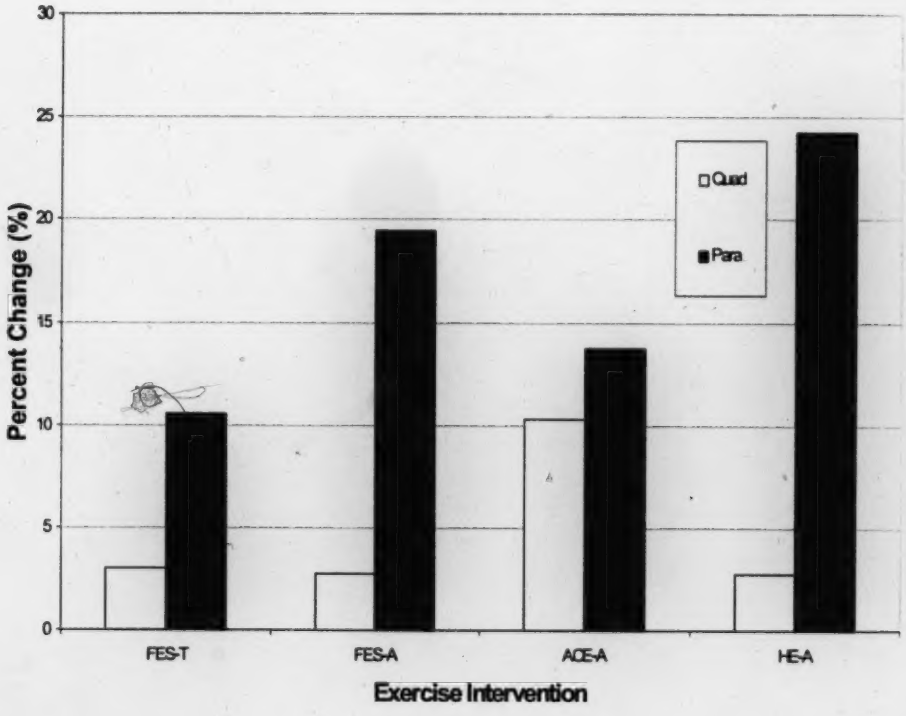


Figure 4.8. Percent change in LDL levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

TG: Quads decreased (-29%) with FES-A, (-26%) ACE-A, and (-10%) HE-A never returning to pre-training levels (see Figure 4.9). In Paras, TG levels decreased with FES-T (-37%); increased to nearly (~10 %) baseline levels with FES-A, and then decreased with ACE-A (-17%), and HE-A (-30%).

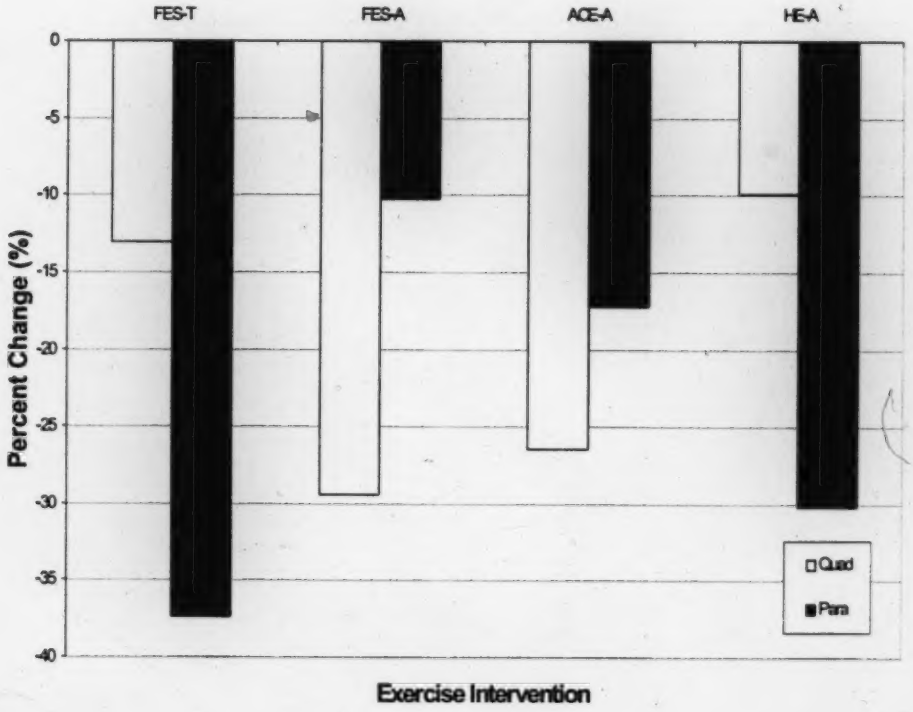


Figure 4.9. Percent change in TG levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

TC: Levels did not change for Quads, but increased with FES-T (8%), FES-A (11%) and HE-A (16%) in Paras (see Figure 4.10).

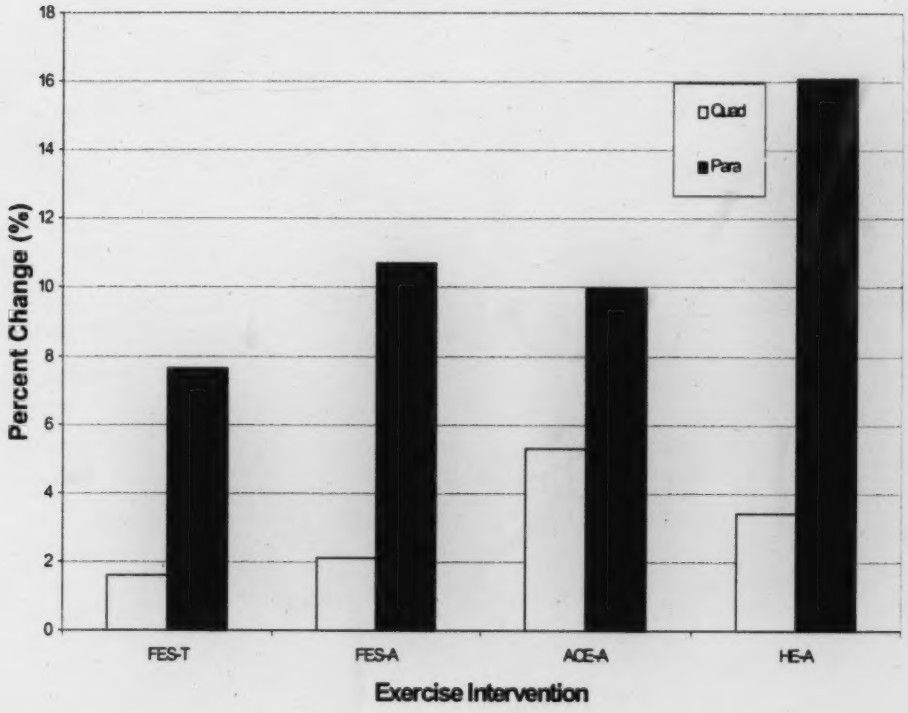


Figure 4.10. Percent change in TC levels in Quads versus Paras after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Dietary Analysis

Analyses showed that consumed calories and fat grams were significantly changed ($p=0.054$ and $p=0.055$). Following two tailed t-tests analyses for paired samples, consumed carbohydrates and fat increased from the second 3d dietary record (DR) to the third 3d DR ($p=0.010$, $p<0.017$ and $p=0.011$, $p<0.017$, respectively) (see Table 4.3). No other statistical findings were found. In the following section, a descriptive analysis is provided on each subject discussing lipids and lipoproteins, and diet.

Table 4.3

Means and Standard Deviations for all Diet Variables

means & standard deviations		
First 3d DR	Second 3d DR	Third 3d DR
avcarb1	avcarb2	avcarb3
248.42 (84.68)	184.17 (32.45)	221.29 (35.25)
avfatg1	avfatg2	avfatg3
74.21 (36.56)	52.97 (15.76)	70.70 (24.53)
avfatpc1	avfatpc2	avfatpc3
30.58 (9.75)	29.83 (7.61)	32.21 (8.86)
avprot1	avprot2	avprot3
80.62 (42.39)	58.07 (12.17)	70.64 (25.21)
avp/s1	avp/s2	avp/s3
0.57 (0.20)	0.52 (0.25)	0.72(0.22)
cal1/wt1	cal2/wt2	cal3/wt9
24.32 (6.93)	19.41(8.43)	23.41 (7.60)

Note: 1,2,3: correspond to the first, second and third dietary records that were collected at baseline, after 8 weeks, and after 17 weeks of the study. Variables: avcarb = average carbohydrates, avfatg = average fat (g) consumed, avfatpc = average fat (%) consumed, avprot = average protein consumed, avp/s = average poly/saturated fat ratio, cal/wt = average calories per weight. Cal/ wt ratio can be particularly useful in determining whether subjects increased calories relative to weight to compensate for energy expenditure.

Single Subject Analysis (lipids, dietary analysis, and summary)

This section discusses percent change in detail and includes absolute values that have clinical significance. Percent changes that have clinical significance are considered significant changes. Absolute values and relative percent change are provided at the end of the chapter (see Tables 4.9-4.34).

Subject #1:

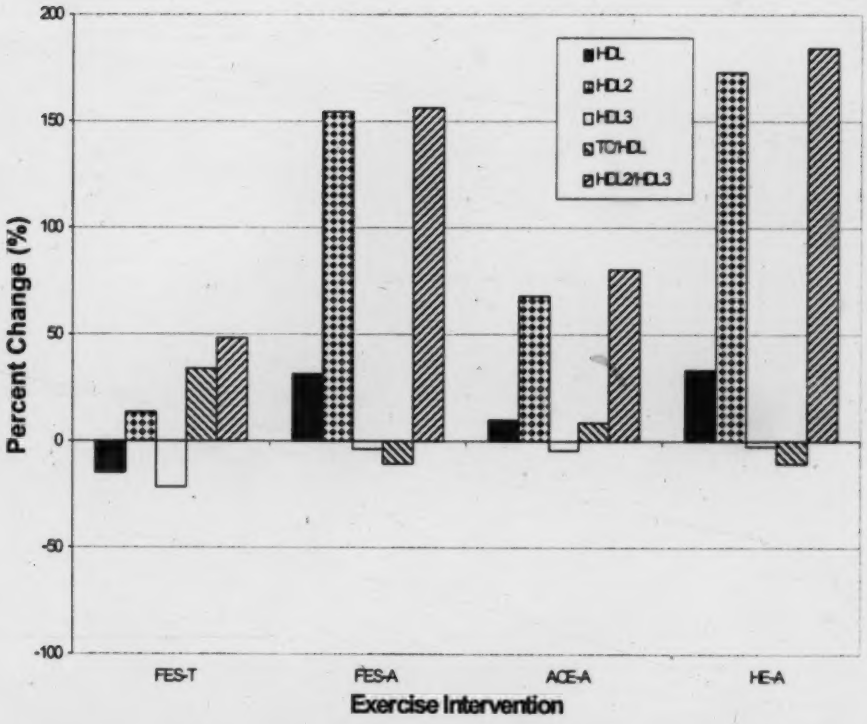


Figure 4.11. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#1) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

HDL levels (see Figure 4.11) increased (6%) after 17 weeks of the study. This change was attributed mostly to increases after FES-A (31.19% from baseline) despite the decrease (-15 %) after performing FES-T. Additional increases occurred with HE-A (21%) leading to a 33% increase overall. On the other hand, ACE-A levels decreased (-19% from rest), but levels remained 10% above baseline overall. Increases in HDL during rest (17% after R_1, 18% after R_3) suggest that the rest period may have not been long enough for levels to return to baseline.

HDL_2: The largest increase in HDL_2 occurred after HE-A (172% from baseline; 15% from R_3)(see Figure 4.11). This increase may be attributed to HDL_2 increases of 136% from baseline after R_3. As shown (Figure 10), FES-T (14%) and FES-A (154%) also increased HDL_2 levels, but ACE-A and R_4 decreased levels by 34% and 45%, respectively. Due to large increases as a result of exercise, HDL_2 increased 50% overall.

HDL_3 levels did not change except for a slight decrease (-22%) after FES-T (see Figure 4.11). Levels tended to return back to pre-training levels between interventions. It is perhaps notable to mention that HDL_3 levels tended to decrease 5-10% with exercise and return to normal levels during rest.

The HDL_2/HDL_3 pattern modelled HDL_2 (see Figure 4.11). Overall, the ratio increased after FES-T (48%), FES-A (156%), and HE-A (184%). The ratio decreased after ACE-A (-25%), however levels remained 80% above baseline. Resting levels suggest that particularly FES-A and ACE-A had lasting positive effects on this ratio whereas HE-A may not have for the ratio was 60% over baseline after R_4. Although It is difficult to describe the effect of training on this ratio due to the increasing levels after one week of rest.

TC/HDL levels increased post FES-T (34%), and ACE-A (14%) and decreased post FES-A (-22%), and HE-A (3%) from resting levels to be 13% over baseline in R_4(see Figure 4.11). Rest levels tended to overcompensate for changes in the direction of baseline levels.

LDL levels did not change (±5%) (see Figure 4.12).

TG levels tended to vary with exercise interventions (see Figure 4.12). All TG levels decreased to (~-26% overall) following acute exercise, but FES-T increased TG by 8%. The greatest decreases from rest occurred after FES-A (-50%) and HE (-40%).

TC levels increased 8% over the course of the study (see Figure 4.12). Levels remained somewhat consistent except for the a 11% increase post FES-A.

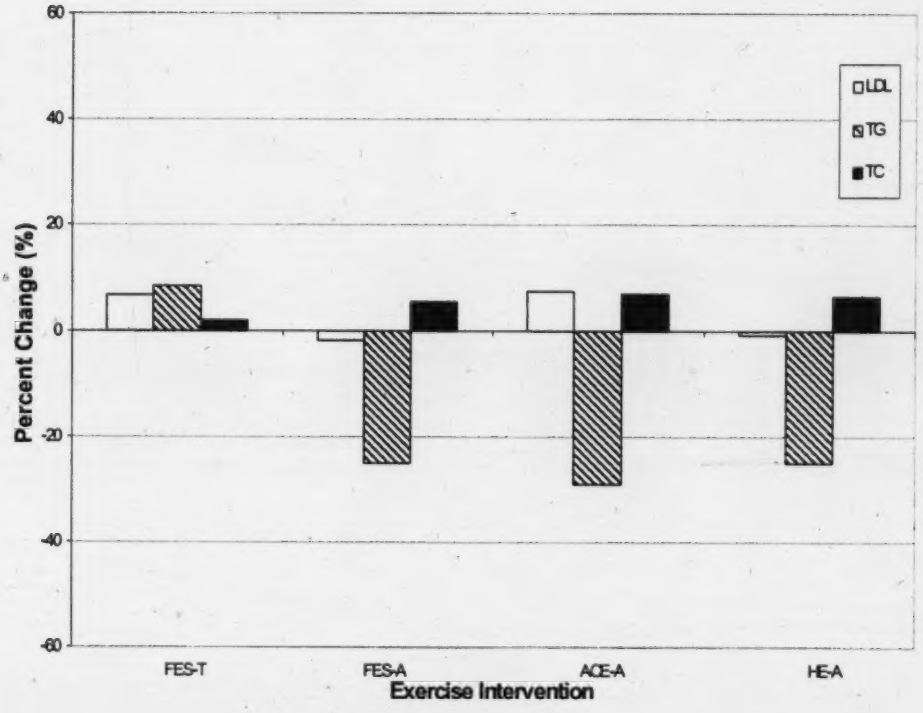


Figure 4.12. Percent change in LDL, TG, and TC in a subject (#1) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Dietary Analysis

After 17 weeks of the study, there were no changes in calories, protein, and carbohydrates. However percent fat increased 17% from baseline in the last dietary record and grams of fat increased in the second and third dietary record by 14 and 12%, respectively. Despite fat increases, this subject did not increase weight throughout the study.

Summary

Data showed that exercise altered levels from baseline in all cases. FES-A and HE-A improved HDL, HDL_2, HDL_3, TG, and TC/HDL to a greater extent than FES-T and ACE-A. In fact, graphed observations indicate that FES-T and ACE-A both had negative implications on lipid-lipoprotein profile. After FES-T, HDL_2 levels and the HDL_2/HDL_3 ratio improved, whereas HDL, HDL_3, TG, LDL, TC levels and TC/HDL ratio did not. Similarly, ACE-A decreased HDL, HDL_2, and HDL_2/HDL_3 and increased TC/HDL and LDL.

Therefore, HE-A or FES-A were preferred exercise interventions in comparison to FES-T and ACE-A.

Subject #2:

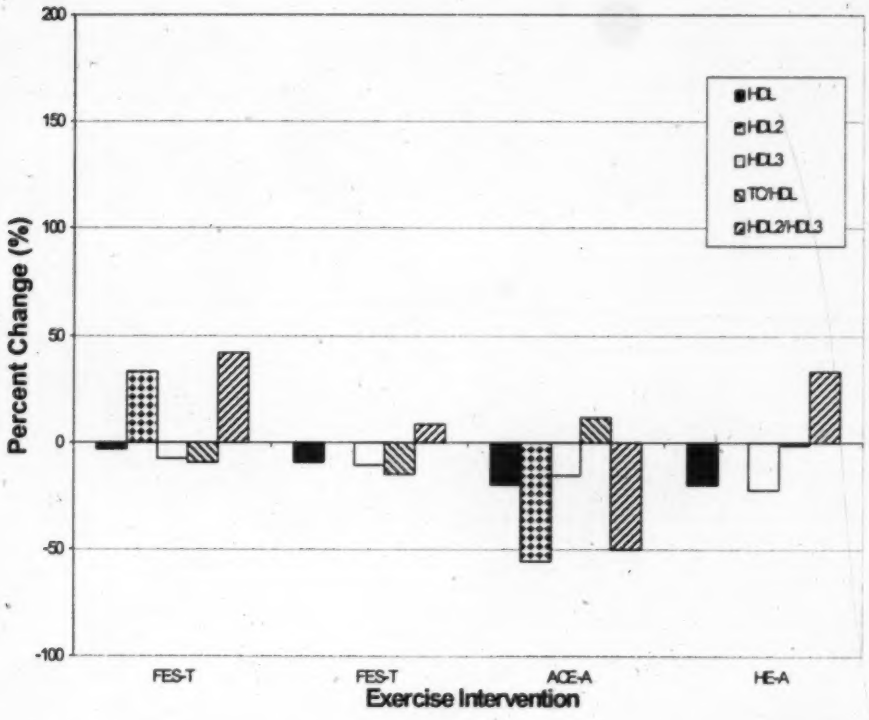


Figure 4.13. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#2) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

HDL levels in subject # 2 were 0.85 mmol/L (see Table 4.7) which suggests that this individual was at risk for CVD (see Figure 4.13). Furthermore, levels remained at risk throughout the study. HDL levels remained unchanged after FES-T and R_1, but were below baseline after FES-A (-9%), ACE-A (-20%) and HE-A (-20%). ACE-A and HE-A increased HDL levels, but were unable to overcome decreased levels (-20%) found after R_2. Therefore, HDL levels were depressed 10% overall after R_4.

HDL_2 levels were depressed in this subject (see Figure 4.13). Highest levels were reached after FES-T (33%), but levels dropped to 0.04 mmol/L (-56% overall) following ACE-A and to 0.00 mmol/L after R_3. After performing HE-A, levels increased to baseline levels (0.09mmol/L) indicating no change overall.

HDL_3 remained depressed (~ -12%) (see Figure 4.13) throughout exercise training to reach lower than baseline levels (-10%) after R_4. HDL_3 decreased after training with ACE-A (-16%) and HE-A (-22%) while resting levels remained depressed, so overall levels were 10% below baseline.

HDL_2/HDL_3 ratio increased after FES-T (42%), FES-A (8%) and HE-A (33%) overall, but reached zero after R_2 and R_3 (-100%) (see Figure 4.13). Levels also decreased after R_4 (-19%) but levels were 8% above baseline.

TC/HDL ratio decreased from baseline levels after FES-T (-10%), FES-A (-15%), and increased after ACE-A (11%) (see Figure 4.13). Resting levels attempted to return to baseline, but were unsuccessful so that levels were depressed by 10% after R_4.
LDL levels decreased after FES-A (-15%) and HE-A (-17%), and increased after ACE-A (9%) (see Figure 4.14). Rest levels fluctuated ±5% from baseline except for after R_4 where levels were 10% below baseline.

TG values decreased after FES-T (-37%) and FES-A (-54% from baseline) (see Figure 4.14). Increases occurred after ACE-A (33% from rest) and HE-A (76% from rest) but overall levels were depressed 54% and 18%, respectively. As TG levels were depressed (36-68%) during the entire study, it is not surprising that TG values were nearly half (-45%) baseline levels after R_4.

TC remained unchanged (±10%), despite a large decrease from baseline after FES-A (-19%) and HE-A (-17%) (see Figure 4.14).

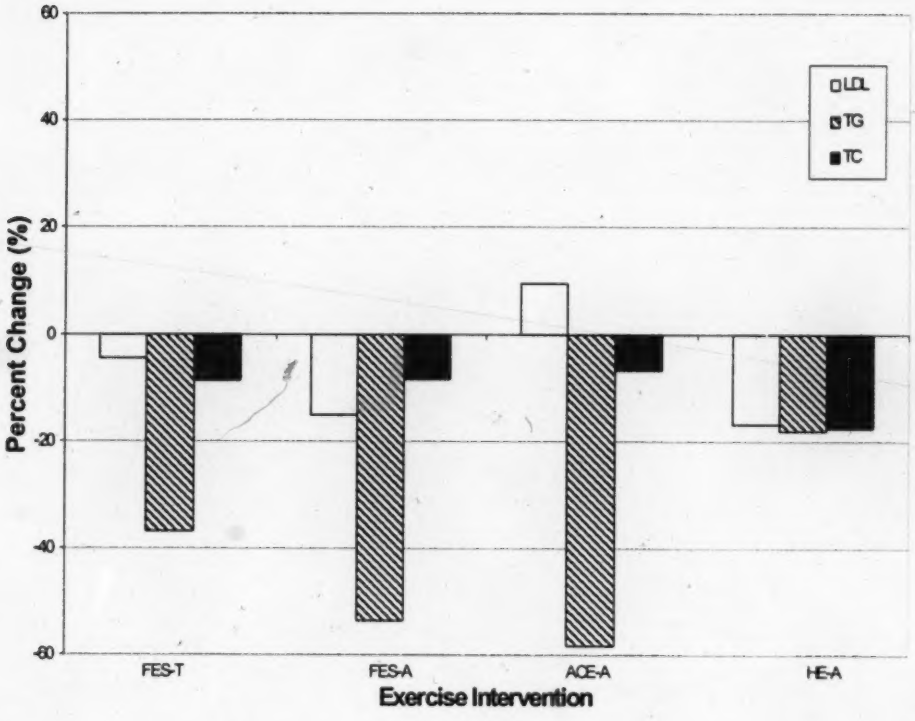


Figure 4.14. Percent change in LDL, TG, and TC in a subject (#2) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Dietary Analysis

This subject gained weight (3.2%) after HE-A training. This corresponds with a 57% increase in total calories from the end FES-T to R_4 to result in an 53% increase in calorie/weight ratio. Also carbohydrate consumption increased by 53%, fat grams increased by 64% (36% overall) and average polyunsaturated/saturated fat ratio decreased 21%. Therefore weight gain was attributed to an increase in energy consumption. This weight gain can perhaps explain why there were no increases in HDL levels after training.

Summary

This subject experienced slight increases in HDL_2 and HDL_2/HDL_3 ratio after FES-T and HE-A. However, training effects on HDL and its subfractions were mostly negative, particularly with ACE-A. ACE-A decreased HDL_2 and HDL_3 to subsequently decrease the HDL_2/HDL_3 ratio to its lowest value. In addition, LDL, TG, and TC levels decreased with almost every intervention, except for ACE-A where LDL levels increased. Therefore, despite the largest decreases in TG, ACE-A was the least effective exercise in terms of improving lipid-lipoprotein profile.

Subject #3:

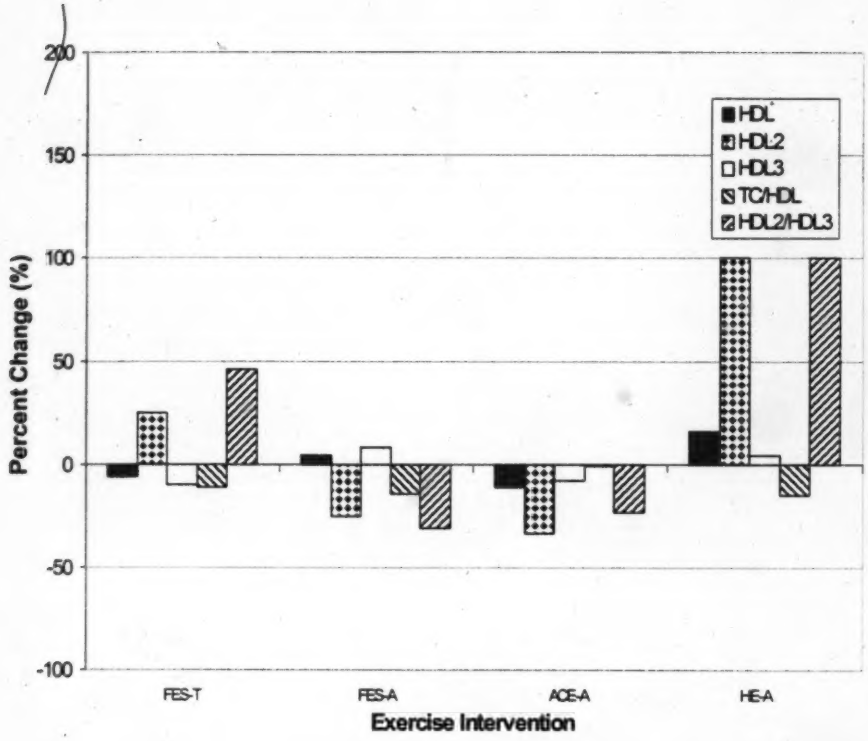


Figure 4.15. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#3) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

HDL levels fluctuated from healthy levels (1.17mmol/L) to levels (0.87 mmol/L) (see Figure 4.15) associated with increased risk for CVD. Levels did not deviate from baseline with FES-T, FES-A, and ACE-A, but increased after HE-A (21% from R_3; 16% from baseline). Levels decreased below baseline after R_2 (1.05-0.87 mmol/L; -14% from baseline) and also after R_4 (1.01-0.88 mmol/L; -13% from baseline).

HDL_2 levels increased 100% from baseline after HE-A (0.11-0.24mmol/L; 118% from R_3)(see Figure 4.15). In fact, HE-A was the only exercise intervention able to

double baseline levels. FES-T also increased HDL_2 levels but only by 25%. Levels increased after ACE-A (0.01-0.08 mmol/L; a 700% from R_2), but remained 33% below baseline. Levels reached their lowest value in R_2 (0.01 mmol/L; -92% below baseline).

HDL_3 levels decreased after FES-T (-10% overall) and R_4 (-11% overall), however there were no other notable changes throughout the study (see Figure 4.15). Levels reached their highest value after performing FES-A (8% above baseline). ACE-A did not change HDL_3 levels.

The TC/HDL ratio for this subject at baseline was 6.70 (see Table 4.16) which is considerably high relative to CVD risk levels. Although FES-T, FES-A, and HE-A decreased levels to below 6.00, rest tended to return levels to baseline so that they were 6% above baseline after R_4 (see Figure 4.15). ACE-A had no effect on these levels.

HDL_2/HDL_3 ratio modelled the same kind of pattern as HDL_2 levels where this ratio nearly reached 0 in R_2 and increased 900% following ACE-A and 100% following HE-A (see Figure 4.15). Despite these large changes relative to resting levels, this ratio decreased 15% relative to baseline levels. Reasons for this decrease can be attributed to large decreases after FES-A (-31% from baseline) and its subsequent R_2 (-92% from baseline).

LDL levels were at risk for CVD increasing from 4.38mmol/L at baseline to 4.87 mmol/L (11%) after R_4 (see Table 4.22 and Figure 4.16). This increase was attributed to a 16% increase after R_1 (4.36-5.09 mmol/L) and a 17% increase after HE-A (4.79-5.12 mmol/L). As levels remained 7% above baseline following FES-A until performing HE-A, one can assume ACE-A had no effect on LDL levels.

TG values remained within 1.55-2.00 mmol/L range (see Table 4.22) except for after R_4 where the TG levels increased (1.96-2.40 mmol/L; 22% from to R_3; 19% overall)(see Figure 4.16). Therefore, TG levels increased from low risk to above risk levels after one week of rest following HE-A. Interestingly, only HE-A raised (19%) TG levels above baseline whereas FES-T, FES-A, and ACE-A all decreased TG levels (-12%, -22%, and -20%, respectively).

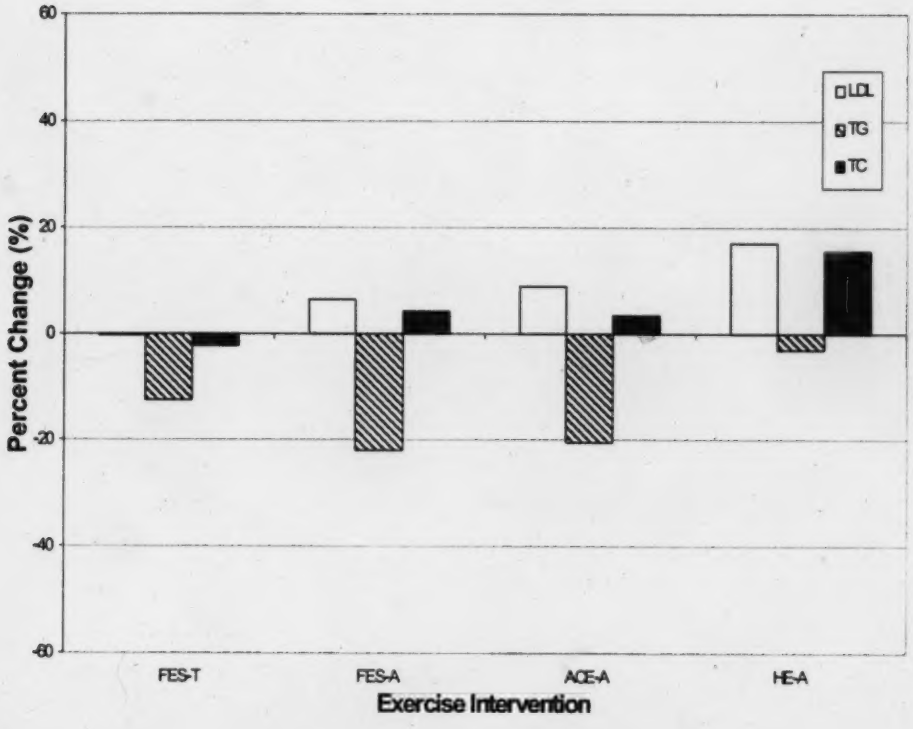


Figure 4.16. Percent change in LDL, TG, and TC in a subject (#3) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

TC levels (5.79 mmol/L) were at borderline high risk for CVD at baseline (see Table 4.28). Levels were negatively influenced by exercise and especially after HE-A (6.09-6.68 mmol/L; 10 % from R_3; 15% above baseline) placing this individual at high risk (>6.20 mmol/L) (see Figure 4.16). Levels decreased to borderline risk after R_4, but were 7% above baseline.

Dietary analysis

This person lost 3.3% of initial body weight, where the greatest decrease occurred after FES-T (-5.6%) and was maintained up to HE-A. This corresponds to the 43% decrease in caloric consumption following FES-T. However, after FES-T, caloric consumption increased 48% (-16% overall). Although it is difficult to pinpoint where the increase in consumption occurred, the subject increased weight only after HE-A exercise. Calories relative to weight also increased 44% from FES-T. In fact, protein, carbohydrate, fat in grams and percent, all increased in the third dietary record relative to the second dietary record. Overall protein (13%) was the only substrate that increased above baseline levels.

Summary

At baseline, this individual was at risk for CVD based on TC, TC/HDL, LDL, and TG. Although exercise positively influenced HDL, HDL_2, and TC/HDL ratio at a clinical level, one week of rest was able to reverse this effect. This was evident during R_2 and R_4 for HDL, HDL_2, and TG. Graphed observations suggest that ACE-A had a negative impact on the lipid-lipoprotein profile, however decreases in values occurred during rest and not as a result of ACE-A. Therefore, even though exercise was beneficial it did not have any long term effects in this subject.

In terms of exercise effects, FES-T exercise increased HDL_2 levels and HDL_2/HDL_3 ratio and decreased TC/HDL ratio and LDL, TG, and TC levels. Slight decreases were also evident in HDL and HDL_3. In contrast, FES-A increased HDL and HDL_3, but decreased HDL_2 and HDL_2/HDL_3 ratio. HE-A improved HDL, HDL_2, and TC/HDL ratio, however it also increased TC and LDL levels to a much greater extent than all other interventions. Of note, HE decreased TG overall, however this decrease was less compared to other interventions.

As HE-A elicited superior improvements in HDL, HDL_2, HDL_2/HDL_3 and TC/HDL, HE-A was perhaps the best type of exercise for this individual as a way to reduce risk for CVD.

Subject #4:

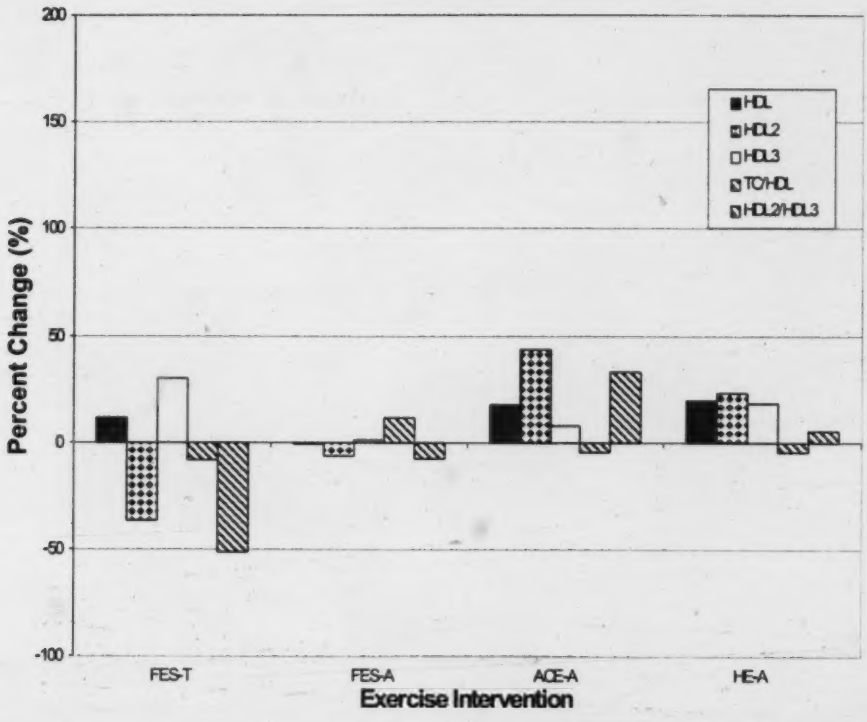


Figure 4.17. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#4) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

HDL levels increased after FES-T(11%), ACE-A (13% from R_2; 18% overall), and HE-A (28% from R_3, 20% overall) (see Figure 4.17). Rest levels were all within ± 5%, therefore suggesting that HE-A elicited the greatest increase.

HDL_2 levels overall decreased after FES-T (-37%), and increased after ACE-A (43%) and HE -A (23%) (see Figure 4.17). Notably, the largest increase (48% from R_2) occurred in ACE-A. Increases (48%) also occurred after HE-A, but the overall increase was reduced due to decreased levels in R_3.

HDL_3 levels did not change except for increases after FES-T (30%) and HE-A (18 % overall). Rest tended to bring levels back to baseline, with the exception of R_2 (see Figure 4.17).

TC/HDL levels overall decreased after FES-T(-8%), ACE-A (-4%; -13% from R_2), and HE-A (-5%) (see Figure 4.17). Levels increased after FES-A (12%) and R_4(10%).

HDL_2/HDL_3 decreased overall after FES-T (-51%), and increased after ACE-A (33%; 49% from R_2) and HE-A (5%) (see Figure 4.17). Although rest periods tended bring levels close to baseline, HDL_2/HDL_3 ratio increased 22% from HE-A and 28% overall after R_4.

LDL levels increased (3.20-3.81 mmol/L) after acute training (see Table 4.22). LDL levels increased to CVD risk levels after performing FES-A (3.78 mmol/L; 18% overall) ACE-A (3.69 mmol/L; 15% overall) and HE-A (3.78 mmol/L; 18% overall) (see Figure 4.18). Levels decreased after R_3 to reach baseline levels, but levels after R_4 did not change from HE-A so that levels remained 19% above baseline.

TG levels decreased overall after FES-T(-44%), FES-A (-33%), ACE-A (-39%), and HE-A (-50%) (see Figure 4.18). Rest levels remained depressed (>20%) throughout the study. Only in R_4, one week after performing HE-A, did TG levels return to baseline levels (91% increase from HE-A; -4% overall).

TC levels increased 14% overall with the largest increase occurring after HE-A exercise (18% from R_3; 13% overall) (see Figure 4.18). Levels tended to increase during exercise and rest except for after R_3 where TC levels dropped 14% relative to ACE-A (-4% overall).

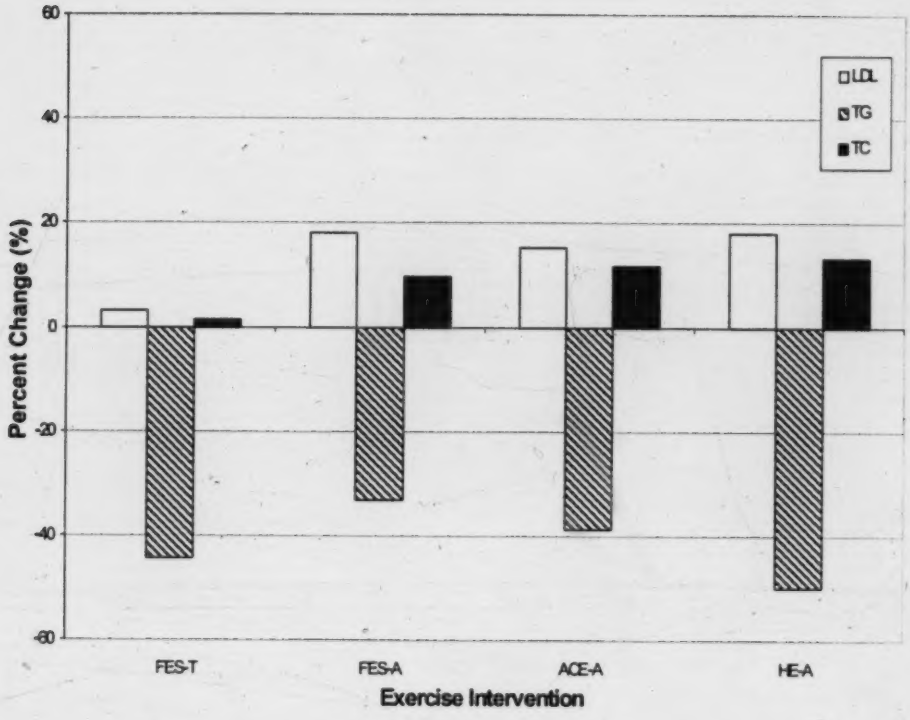


Figure 4.18. Percent change in LDL, TG, and TC in a subject (#4) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Dietary analysis

Overall, this subject increased calories (11%), calories/weight ratio (12%), carbohydrates (16%), and poly/sat fat ratio (234%), and decreased percent fat (-17%). Increased calories and calories/weight ratio were attributed to FES-T training. Increased carbohydrates and poly/sat fat ratio combined with decreased percent fat could be attributed to acute training, however no weight loss occurred.

Summary

This subject was unable to pedal more than two minutes on the FES-LCE, therefore it is not surprising that the largest improvements in lipid-lipoprotein profile occurred with ACE-A and HE-A which both used the upper body to exercise.

HE-A increased HDL and HDL_3 levels and decreased TC/HDL ratio, however ACE-A had higher HDL_2 levels. Despite improvements with ACE-A and HE-A in terms of HDL and its associated subfractions and ratios, LDL and TC levels increased during these interventions. On another note, FES-T also elicited improvements in HDL, HDL_3, TC/HDL, and TG, but more importantly, TC and LDL levels increased only slightly.

Since HDL levels are protective in terms of CVD, the increased HDL levels with ACE-A and HE-A may have been of more importance than the increased LDL and TC levels (see Chapter 5)

Subject #5:

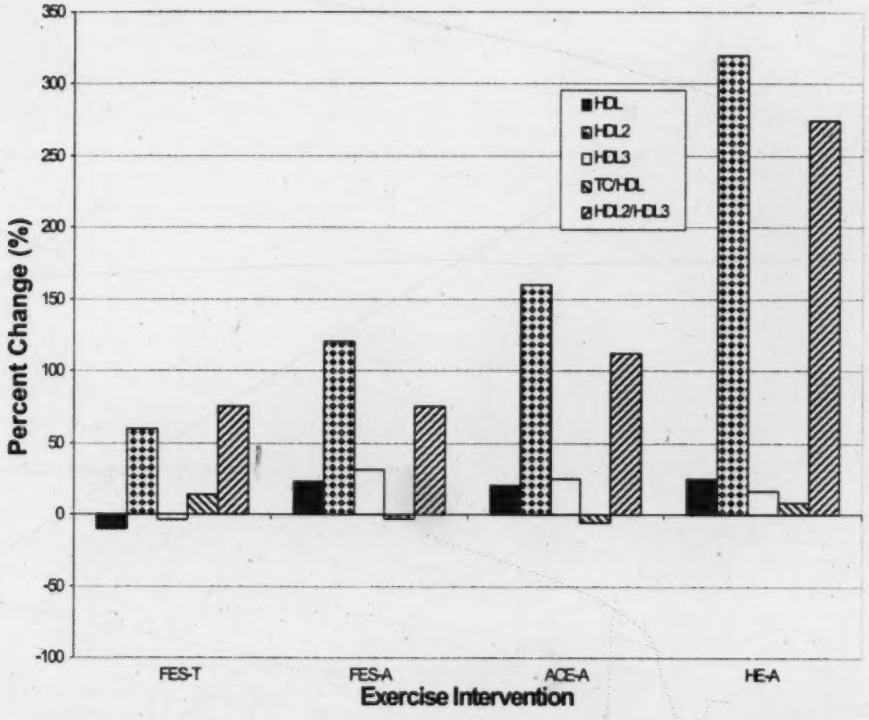


Figure 4.19. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#5) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels. Note the change in scale from 200 to 350 % on the y axis due to the larger increases in HDL_2.

HDL levels decreased after FES-T (0.73-0.66 mmol/L; 10%), and increased after R_1 (0.84 mmol/L; 23% from baseline) (see Figure 4.19). Acute exercise training decreased or maintained HDL levels from resting levels. FES-A maintained levels at 0.90 mmol/L, and ACE-A and HE-A decreased levels by 3% and 5%, respectively. Rest periods raised HDL to make levels 30% (0.95 mmol/L) above baseline after R_4.

HDL_2 levels increased 60,120,160 and 320% from baseline after performing FES-T, FES-A, ACE-A, HE-A, respectively, illustrating a 0.20 mmol/L increase (400%) after 17 weeks of the study (see Figure 4.19). Although levels increased, the largest increases occurred during rest 240, 180, 440, and 400% in R_1, R_2, R_3, and R_4 respectively.

HDL_3 levels decreased after performing FES-T (-3%) but increased by 22% after R_1. FES-A, ACE-A and HE-A all increased HDL_3 levels by 32%, 25%, and 17%, respectively from baseline(see Figure 4.19). Rest levels tended to stay elevated so that after R_4 levels were 17% above baseline levels.

TC/HDL ratio had only two peaks; one after FES-T (14%) and another after performing HE-A (18% from R_3, 8% from baseline) (see Figure 4.19). Exercise tended to increase this ratio while rest would decrease levels. Levels after 17 weeks were 13% below baseline.

HDL_2/HDL_3 ratio followed approximately the same pattern of increase as the HDL_2 levels, however increases were even larger. This ratio increased from 0.08 to 0.36 mmol/L after 17 weeks of the study (See Table 4.19). Again most of the increases occurred during rest (187, 125, 387, and 350% after R_1, R_2, R_3, and R_4, respectively (see Figure 4.19). Exercise decreased levels relative to resting levels, however FES-T and FES-A increased 75%, ACE-A 112%, and HE-A 275% relative to baseline levels.

LDL levels did not significantly change, except for increases after HE-A (17% from R_3, 20% overall) (See Figure 4.20). Levels were 6% below baseline after R_4.

TG levels decreased overall after FES-T (-32%) and FES-A (-29%) and increased after HE-A (32%)(see Figure 4.20). Resting levels attempted to return to baseline and levels were 4% below baseline in R_4.

TC levels did not change except for after HE-A when levels increased 12% from R_3 and 22% overall (see Figure 4.20). Levels were 2% above baseline after R_4, indicating no change.

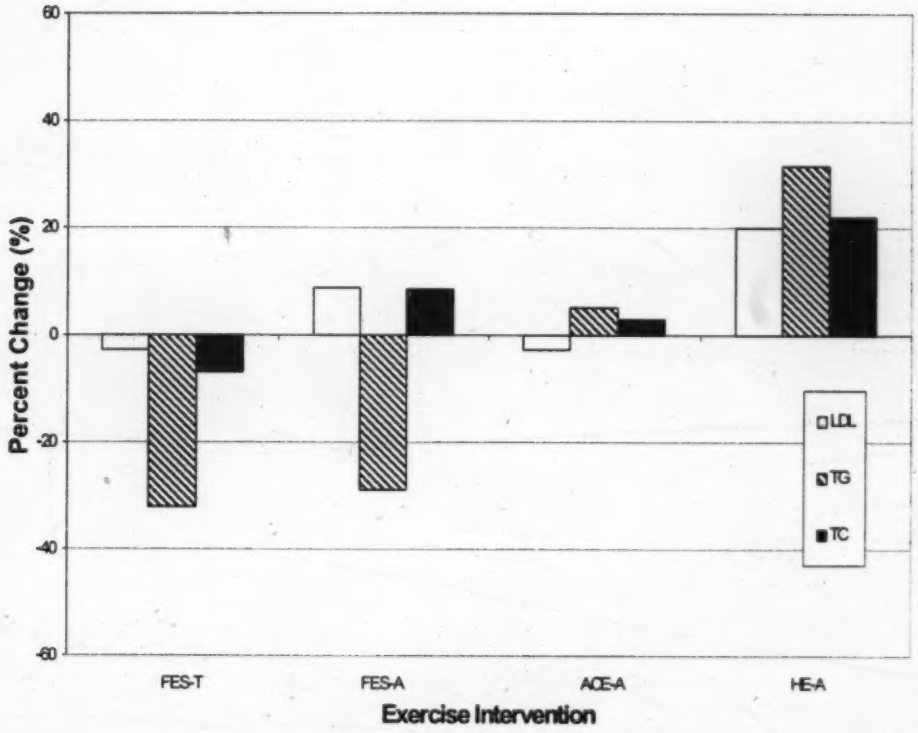


Figure 4.20. Percent change in LDL, TG, and TC in a subject (#5) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Dietary analysis

Although there was a 12% increase in caloric intake and a 11% increase in calories relative to weight, overall this subject lost 7% of total body weight. This weight loss appeared to be gradual with the greatest decrease (-4%) occurring with FES-T. After FES-T (second dietary record) calories, carbohydrate consumption and poly/sat ratio had decreased and percent fat had increased. Therefore it seems that the decrease in weight could have been attributed to a decrease in calories.

In the third dietary intake, calories, calories/weight ratio, carbohydrate, protein, and fat grams increased and percent fat remained the same, however weight decreased another 3%. Therefore it is possible that exercise and energy expenditure more than diet affected weight loss during the acute exercise phases of the study.

Summary

This particular subject improved remarkably over the course of the study. HDL, HDL_2, HDL_3, and HDL_2/HDL_3 progressively increased with FES-T, FES-A, ACE-A, to reach their maximum after HE-A. HE-A also increased LDL, TG, and TC levels, however these returned to baseline levels after R_4. The fact that LDL, TG and TC levels returned to baseline whereas HDL particles did not, may have been due to mobilized free fatty acids from adipose and muscle tissues as a result of exercise (see Chapter 5).

Subject #6:

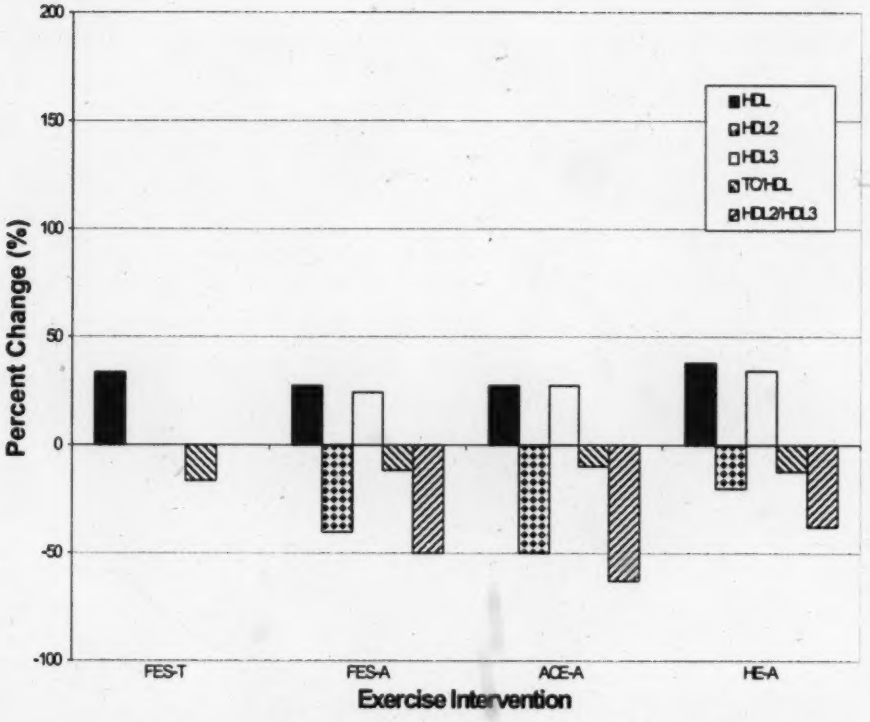


Figure 4.21. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#6) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Subject #6 was expected to have some liver damage due to a suicide attempt during the study.

HDL: HDL increased 33% after FES-T, 27% after FES-A, 27% after ACE-A, and 38% after HE-A (see Figure 4.21). Despite these increases, this person remained at risk during the study except for after HE-A when levels rose to 0.91 mmol/L. Levels were 0.74 mmol/L after R_4 indicating a 12% increase from baseline. Resting levels attempted to return to baseline, but remained more than 12% above baseline.

HDL_2 levels fluctuated between 00-0.15 mmol/L (see Table 4.10) throughout the study and were 50% below baseline after R_4 (see Figure 4.21). HDL_2 levels reached their lowest value after R_1 and peaked in R_2 (150% relative to FES-A; 50% overall). FES-A and HE-A (60% from R_3) increased levels, whereas ACE-A (-67% from R_2) decreased levels, however all values remained at -40, -50, and -20% below baseline.

HDL_3 increased in FES-A (24% overall), ACE-A (21% from R_2; 28% overall), and HE-A (12% from R_3; 34% overall) to be 11% above baseline after R_4 (see Figure 4.21). Rest levels attempted to return to baseline but remained elevated.

TC/HDL ratio was at high risk levels (7.02) at baseline and fluctuated with exercise and rest periods (see Table 4.16). The TC/HDL ratio decreased from 7.02 to 5.85 (-17% overall) after FES-T, (6.15 ;-12% overall) after HE-A, and also after FES-A and ACE-A (-11 and -10%, respectively) (see Figure 4.21). Rest ratios tended to increase towards baseline but remained depressed. Overall levels were depressed by 8% after R_4.

HDL_2/HDL_3 ratio showed similar trends to the HDL_2. The HDL_2/HDL_3 ratio increased (187% from FES-A; 44% from baseline) after R_2 and (43% from R_3; -37% from baseline) after HE-A, but incurred large decreases after R_1 (0.00), and ACE-A (-74% from R_2; -62% overall) (see Figure 4.21). Rest increased the ratio, but it was 56% below baseline after R_4.

LDL levels increased overall after FES-T (14%), FES-A (34%), ACE-A (36%), and HE-A (51%) (see Figure 4.22). Levels were above CVD risk levels following FES-T training to reach 4.51 mmol/L after R_1 (see Table 4.22). Rest levels remained high after each intervention except for after R_4 where levels dropped 22% to be 18% above baseline.

TG levels decreased overall after FES-T (-21%), FES-A (-13%), ACE-A (-6%) and HE-A (-50%) (see Figure 4.22). Resting levels were very inconsistent, where R_1 and R_3 levels decreased (-28% and -8%, respectively), and R_2 and R_4 levels increased (36% and 13%, respectively).

TC levels were elevated more than 25% over the course of the study to end the study with levels 17% above baseline (see Table 4.22). All exercise interventions increased TC levels particularly HE-A where levels were 37% above baseline. Rest levels also increased so that levels increased to CVD risk levels following R_1 and remained elevated until after R_4.

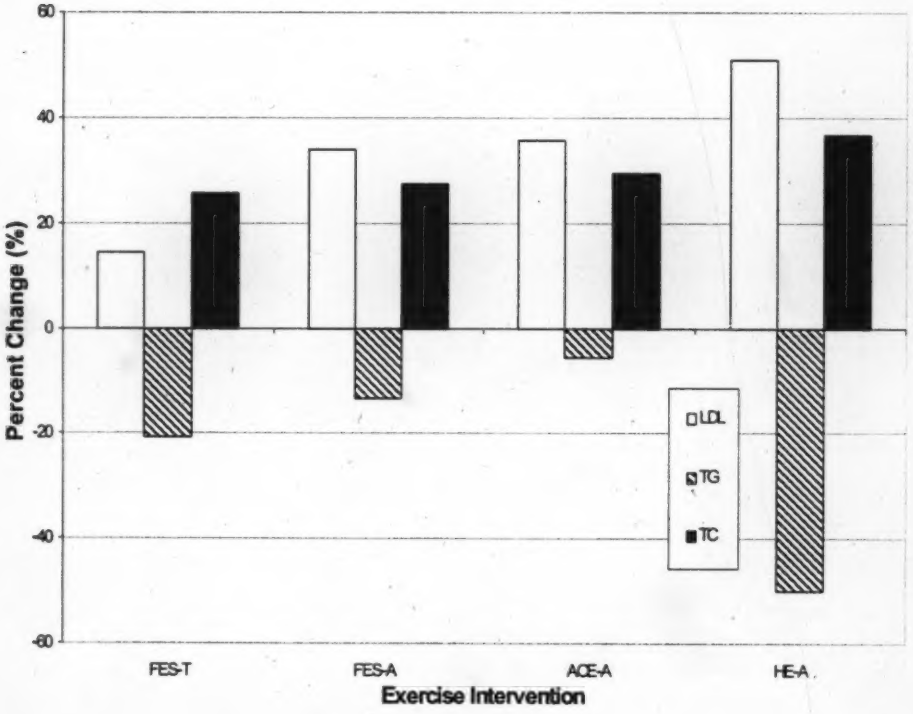


Figure 4.22. Percent change in LDL, TG, and TC in a subject (#6) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels

Dietary analysis

Overall this subject increased percent fat up to 39% of total caloric intake, but also increased poly/sat fat ratio.

Summary

Exercise had very little impact on HDL_2 levels, however HDL levels increased with all interventions. Coincidently, TC and LDL levels also increased. Of note, TC/HDL ratio remained depressed for the duration of the study suggesting that HDL levels increased more than TC levels.

The largest increase in LDL levels occurred with HE-A training while TG levels decreased to their lowest value. HDL and HDL_3 levels increased particularly with HE-A and were consistently above baseline over the duration of the study. HDL_2 levels and HDL_2/HDL_3 ratio also increased with FES-A and HE-A but were not apparent due to large decreases during rest periods.

It is notable to mention that rest levels tended to return post-exercising levels and ratios to baseline. Considering this individual was at risk based on HDL, HDL_2, LDL, TC levels and TC/HDL ratio and exercise improved HDL, HDL_2 and TC/HDL, exercise would be extremely beneficial at reducing CVD risk.

Subject #7:

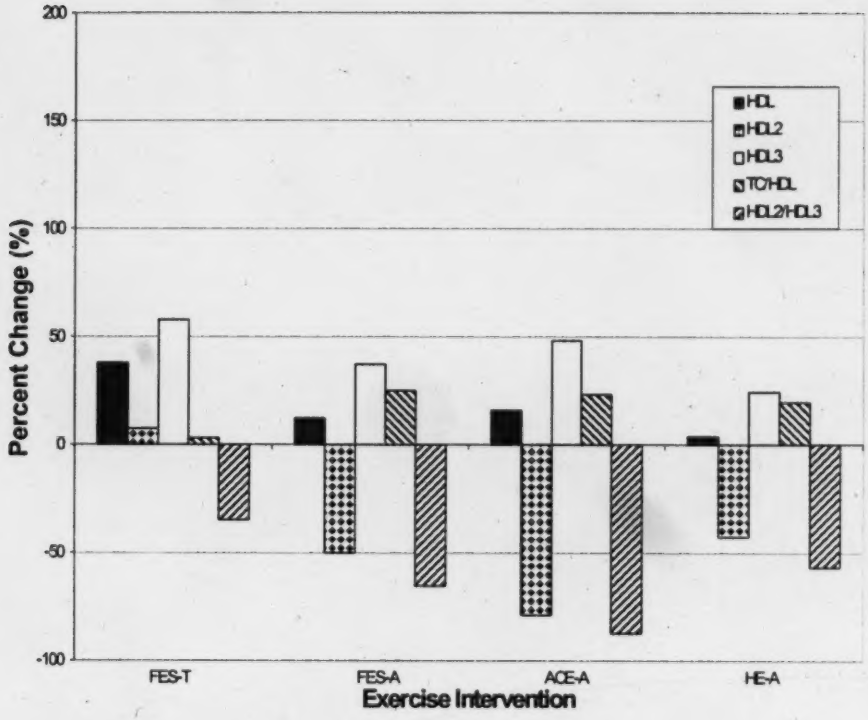


Figure 4.23/ Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#7) with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

HDL levels increased from risk levels (0.82mmol/L) at baseline to healthy levels (1.13 mmol/L; 38%) after performing FES-T (See Table 4.7). After this initial increase in HDL levels, minor peaks occurred during R_2 (6% from FES-A; 19% overall) and R_4 (18% from HE-A; 22% overall) (see Figure 4.23), suggesting that blood levels increased during rest without having sufficient time to return to baseline. ACE-A did not improve HDL levels, however exercise typically decreased HDL whereas rest increased levels.

HDL_2 levels decreased as the study progressed except for after R_4 where levels increased 112% from HE-A; 21% from baseline (see Figure 4.23). HDL_2 levels decreased after FES-A (-22% from R_1; -50% overall), HE-A (-11% from R_3; -43% overall), and to a greater extent after ACE-A (0.08 to 0.03mmol/L ;-62% from R_2; -79% overall).

HDL_3 increased after FES-T (58%), and decreased after FES-A (-10% from R_1; 37% overall), did not change after ACE-A from R_2 (48% overall), and decreased after HE-A (-5% from R_3; 24% overall) (see Figure 4.23). Rest levels remained elevated so that levels after 17 weeks were 34% above baseline.

TC/HDL levels increased overall after FES-A (25%), ACE-A (23%) and HE-A (19%) (see Figure 4.23). Levels remained elevated during rest so that levels were 11% above baseline after R_4.

HDL_2/HDL_3 ratio followed the same pattern as HDL_2, but this ratio decreased (-13%) after R_4 (see Figure 4.23). This ratio decreased overall with FES-T (-35%), FES-A (-65%), HE-A (-56%) and largely with ACE-A (-87%). R_2, R_3 and R_4 increased 12% 267% and 100.00% relative to FES-A, ACE-A and HE-A , respectively but levels remained depressed (~ 50%) relative to baseline.

LDL levels increased after FES-T(10%), FES-A (18%), and ACE-T (17%) relative to baseline (see Figure 4.24). LDL decreased after R_2 (-9%), and R_3 (-11%) in relation to FES-A and HE-A, but levels remained above baseline. After R_4 levels were 6% above baseline.

TG levels increased overall after FES-T(33%), FES-A (15%), ACE-A (45%) and HE-A (8%) (see Figure 4.24). Resting levels remained elevated with the largest increase occurring after R_4 (50% from HE-A; 62% overall). One exception was found after R_3 where levels decreased 36% from ACE-A and 7% overall.

TC levels increased overall after FES-T (18%) and ACE-A (17%), and ACE-A (19%)(see Figure 4.24). However, HE-A decreased TG levels to 3% above baseline. Rest levels (R_1 and R_2) remained elevated, R_3 decreased (-12% from ACE-A) and R_4 increased (9%).

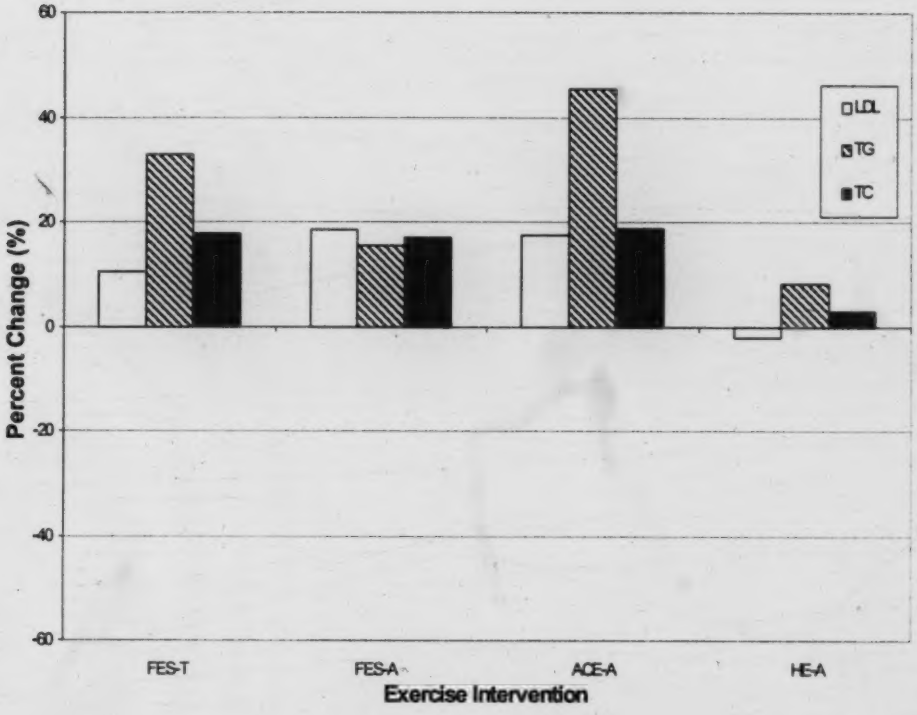


Figure 4.24. Percent change in LDL, TG, and TC in a subject with quadriplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Dietary analysis

Unfortunately, due to poor balance of the subject on the measuring scale, no reliable weight reading was made available for this subject. However, Dietary analysis suggests that this individual should have at least maintained weight. The largest improvements in diet were found after performing eight weeks of FES-T. Caloric intake, carbohydrates and fat all decreased, yet weight did not change. Acute training raised these levels so that overall, calories decreased 4%, carbohydrates increased 5%, fat percent did not change and poly/sat fat ratio increased 164%.

Summary

Acute exercise interventions appear to have decreased HDL levels while rest increased levels. It is unknown whether increases were demonstrating a return to desired levels or a training effect.

HDL, HDL_2, and HDL_3 levels improved to the largest extent with FES-T. However, HDL_2 levels and thus HDL_2/HDL_3 decreased considerably with all other exercise interventions, and increased during resting periods. Also, TC/HDL ratio was reduced with all interventions as a result of increasing TC levels and decreasing HDL levels with training.

LDL and TC levels increased with all interventions except for HE-A and TG levels increased to the largest extent with ACE-A and to the least extent with HE-A. Yet, HE-A resulted in lower HDL and HDL_3 levels than all other interventions.

Based on graphed observations, it is difficult to determine which exercise intervention(s) elicited the best results. However, as HDL levels increased from CVD risk levels to healthy levels, and HDL_2, HDL_3 and TC/HDL levels improved with FES-T, FES-T was the best intervention for this individual.

Subject #8:

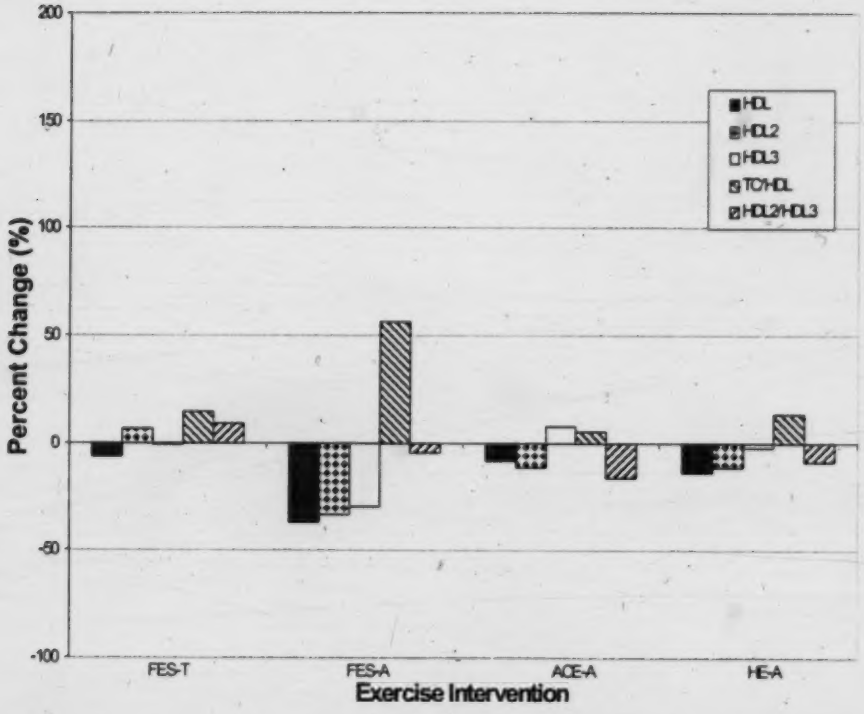


Figure 4.25. Percent change in HDL, HDL_2, HDL_3, TC/HDL, and HDL_2/HDL_3 in a subject (#8) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

This subject is female and tended to have higher HDL levels (1.50 mmol/L) compare to other subjects (1.00 mmol/L).

HDL levels decreased after FES-T (-6%) and FES-A (-23% from R_1; -37% overall)(see Figure 4.25). Rest levels tended to decreased these levels even further. In 17 weeks of exercise, HDL levels dropped 0.23 mmol/L (-15% overall).

HDL_2 levels increased in relation to rest after FES-T(6%), ACE-A (14%) and HE-A (17%), however overall levels were decreased after FES-A(-33%), ACE-A (-11%) and HE-A (-11%)(see Figure 4.25). Therefore FES-T was the only exercise intervention that increased levels above baseline. Rest levels kept levels below -19% so that levels were 21% below baseline after R_4.

HDL_3 levels remained unchanged (1% increase overall) except for a large increase after R_2 (57%) which compensated for the decrease after FES-A (-26% from R_1; -29% overall)(see Figure 4.25).

TC/HDL ratio increased overall after FES-T (14%) and FES-A (56%), and decreased after HE-A (13%)(see Figure 4.25). ACE-A did not affect the ratio. Rest levels were elevated more than 15% so that levels were 26% above baseline after R_4.

HDL_2/HDL_3 levels increased overall after FES-T (8% overall), but decreased after ACE-A (-16%) and HE-A (-8%) (see Figure 4.25). Although exercise increased the ratio in relation to rest (12% with FES-A, 19% with ACE-A, 26% with HE-A), the ratio decreased to a greater extent after rest (-14% with R_1, -29% with R_2, -28% with R_3) so that levels dropped 21% below baseline after R_4.

LDL levels were at CVD risk prior to and during the study (>3.40 mmol/L) (see Table 4.22). Levels decreased after FES-A (-11%), ACE-A (-9%) and HE-A (8%) however increased overall after FES-T (24%), FES-A (16%), ACE-A (5%) and HE-A (10%) (see Figure 4.26). Levels were 28% above baseline after R_4.

TG levels decreased to their lowest value after FES-T (-55.94%) and then increased to 2.60 mmol/L (221% from R_2 levels; 29% overall) after FES-A (see Figure 4.26), placing this individual at CVD risk (<2.4 mmol/L) (see Table 4.25). Levels subsequently decreased after ACE-A (-12% from R_2; -30% overall) and were unchanged until after R_4 where levels decreased 51% below baseline. Rest levels tended to bring values below baseline (-20%).

TC levels were at borderline high CVD risk (5.48 mmol/L) (see Table 4.28) and increased during the study. FES-T increased levels by 9% but returned to baseline following FES-A (see Figure 4.26). No further changes were evident until after R_4 where levels increased 8% above baseline.

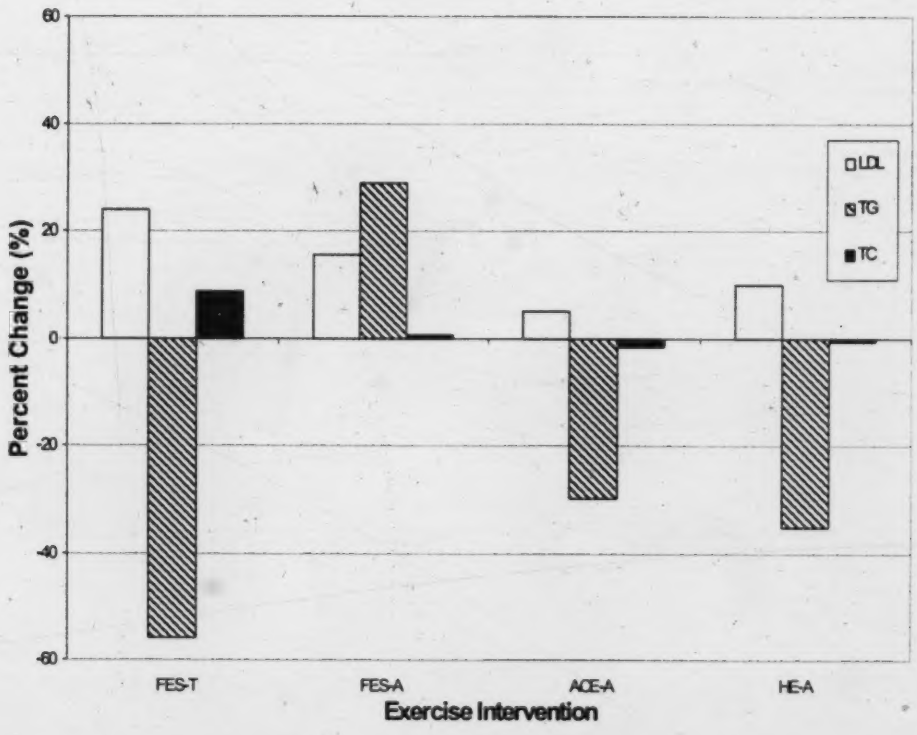


Figure 4.26. Percent change in LDL, TG, and TC in a subject (#8) with paraplegia after performing FES-T, FES-A, ACE-A, and HE-A relative to baseline levels.

Dietary analysis

Subject 8 lost weight (4.4%) after FES-T. Further decreases in weight seemed to follow FES-A and ACE-T, with a .60kg increase after HE-A. After FES-T, subject 8 had decreased total caloric consumption by 13%, calories/weight ratio (-9%), carbohydrate (-

7%), fat percent (-33%), and fat grams (-35%). Poly/sat ratio also increased by 61%. Therefore, it is most certain that this subject lost this weight due to a caloric restriction. In the second half of the study, this subject maintained her weight loss, yet calories increased to 6% below baseline, calorie/weight ratio returned to baseline, and carbohydrates increased. Therefore, weight loss can perhaps be attributed to an overall decrease in fat% (-23%) and fat grams (-30%) with a caloric restriction of 6%.

Summary

HDL, HDL_2, and HDL_3 levels were remarkably higher in this female subject than in all seven male subjects (1.60 mmol/L versus 0.88 mmol/L). After 17 weeks of the study, HDL and HDL_2 levels decreased whereas HDL_3 levels did not change. However these levels were far from being at CVD risk. Notably, FES-T was the only intervention that increased HDL_2 levels.

LDL increased to CVD risk levels after FES-T. TG increased to CVD risk levels after FES-A and remained elevated until after R_4 where levels dropped 50%. TC were at CVD risk levels and peaked after FES-A and R_4.

Based on the results of this study, exercise did not appear to be beneficial for this individual.

Exercise Testing

Table 4.4

Maximal Heart Rate (bts/min), Borg-RPE Scale and peakVO_2 (L/min) during Maximal Testing

Subject #	FES-A			ACE-A			HE-A		
	HR	RPE	VO_2	HR	RPE	VO_2	HR	RPE	VO_2
1	103	12	0.353	120	19	0.605	147	19	0.997
2	89	11	0.571	107	17	0.795	121	18	1.041
3	97	11	0.759	104	17	0.914	104	20	1.682
4	110	11	0.761	164	18	1.335	166	19	1.679
5	108	7	0.749	166	19	1.549	107	20	1.664
6	70	11	1.118	177	18	1.562	178	17	1.867
7	93	13	1.457	105	19	1.622	140	16	1.090
8	114	8	0.656	165	19	1.146	112	17	1.333
Mean	98	11	0.800	139	18	1.190	134	18	1.420
SD	14	2	0.340	32	1	0.388	28	2	0.345
Qmean	96	12	0.785	109	18	0.984	128	18	1.203
QSD	6	1	0.478	7	1	0.444	19	2	0.322
Pmean	101	9	0.821	168	19	1.398	141	18	1.636
PSD	20	2	0.785	6	1	0.198	36	2	0.222

Note: SD = Standard Deviation, Qmean; Pmean = Mean value for Quads and Paras, QSD; PSD = Standard Deviation for Quads and Paras.

Heart rates were significantly higher with ACE-A than with FES-A ($p=0.012$, $p<0.017$), but not between ACE-A and HE-A ($p=0.745$, $p<0.017$) and FES-A and HE-A ($p=0.26$, $p<0.017$) (see Table 4.4).

RPE-values were significantly higher with ACE-A compared to FES-A ($p=0.000$, $p<0.017$) and also with HE-A compared to FES-A ($p=0.000$, $p<0.017$). No significant difference was found between ACE-A and HE-A (see Table 4.4).

Maximal aerobic power measurements were significantly higher with ACE-A compared to FES-A ($p=0.002$. $p<0.017$) and with HE-A compared to FES-A ($p=0.005$, $p<0.017$). No significant differences were found between ACE-A and HE-A ($p=0.120$, $p<0.017$) (see Table 4.4).

Difference between Quads and Paras.

Heart rates were different after performing two tailed t-tests for independent samples between Quads and Paras only when performing ACE-A ($p=0.000$, $p<0.05$). No significant difference between groups was observed for FES-A and HE-A (see Table 4.4).

RPE-values (see Table 4.4) between the two groups were not significantly different at $p<0.05$.

Maximal aerobic power measurements (see Table 4.4) when compared between the two groups were shown to be insignificant at $p<0.05$.

Exercise Training

All subjects completed eight weeks of FES-T and three intense weeks of FES-A, ACE-A, HE-A separated by one week of rest. FES-T required subjects to exercise with FES-LCE three times a week for 30 minutes to complete 24 sessions. The acute training required four consecutive days of exercise starting with FES, followed by ACE, and completed with HE. All acute training was preceded with peak VO_2 and followed by one week of rest. No subject missed any sessions during the acute exercise interventions. Yet, some subjects needed longer than one week during their rest periods in order to get over bladder infections or other illnesses, deal with family issues, or travel on business.

In the first couple of weeks of FES-T, no subject completed more than seven consecutive minutes of cycling. After 5 minutes of rest, most subjects were not able to complete half the cycling time achieved in the first 10 minute period.

An average of 2.5 weeks (median: 3.1 weeks) and 8 sessions (median; 10 sessions) were required in order for subjects to complete 30 consecutive minutes of cycling. One subject completed 30 minutes of cycling after 0.4 weeks (second session), another after 1.4 weeks, a third after 3.5 weeks, and three subjects after 3 weeks of

training. The remaining two subjects were unable to complete more than two minutes of exercise on the FES-LCE throughout the study. These subjects exercised by pushing their legs with their hands to prevent fatigue (<35 rpm) and a two minute cooldown.

Quads had difficulties training with ACE. To make ACE possible, subject's hands were attached to the ACE handles via grip assistance cuffs. However, this was uncomfortable and elicited complaints from all subjects.

Resistance.

Table 4.5

Resistances for FES-T, FES-A, ACE-A and HE-A

Subject#	FES-T	FES-A	ACE-A	HE-A
1	1.0/8 kp	1.0/8 kp	0.30 kg	1/8 kp + 0.3 kg
2	0.2/8 kp	1.0/8 kp	0.20 kg	1/8 kp + 0.2 kg
3	0/8 kp	0/8 kp	0.40 kg	*0/8 kp + 0.4 kg
4	0/8 kp	0/8 kp	1.40 kg	*0/8 kp + 1.2 kg
5	1.3/8 kp	1.5/8 kp	1.20 kg	1/8 kp + 1.3 kg
6	1.0/8 kp	2.0/8 kp	1.20 kg	1/8 kp + 1.5 kg
7	0.2/8 kp	1.0/8 kp	0.95 kg	0/8 kp + 1.0 kg
8	0.4/8 kp	1.5/8 kp	1.20 kg	1/8 kp + 0.9 kg
Mean	0.5/8 kp	0.9/8 kp	0.90 kg	0.8/8 kp + 0.9 kg
SD	0.5/8 kp	0.7/8 kp	0.50 kg	0.5/8 kp + 0.5 kg

Note: The power outputs stated for FES-A, ACE-A and Hybrid-A were in auto mode.

* People who required technician assistance to pedal the FES-LCE

Resistance varied greatly within the group (see Table 4.5). When FES-A and ACE-A combined in HE-A there were very few alterations made to the level of resistance in FES-A and ACE-A individually. Therefore, the total resistance with HE-A was the sum of the moderate intensity load on the ACE-A and the load at which subjects could pedal for 30 minutes on FES-LCE without going into fatigue (<35 rpm).

Work Rate.

Table 4.6

Work rate (W)

Subject#	FES-A	ACE-A	HE-A
1	6.1	7.5	13.6
2	6.1	5.0	11.1
3	0	10.0	10.0
4	0	35.0	30.0
5	9.2	30.0	38.6
6	12.2	30.0	43.6
7	6.1	23.8	25.0
8	9.2	30.0	28.6
Mean(SD)	6.1(4.3)	21.4(12.0)	25.1(12.6)
Qmean(SD)	4.6(3.1)	11.6(8.4)	12.7(9.9)
Pmean(SD)	7.6(5.3)	31.3(2.5)	35.2(7.1)

Note: SD = Standard Deviation, Qmean; Pmean = Mean values for Quads and Paras. The power outputs stated for FES-A, ACE-A and Hybrid-A were in auto mode. Flywheel of FES measured: 1.606m and travelled 5.965 m/revolution. The flywheel for the ACE measured: 1.00m and travelled 1.430 m/revolution.

Work rate was significantly higher with ACE-A than with FES-A ($p=0.008$, $p<0.017$) and with HE-A and FES-A ($p=0.001$, $p<0.017$). No differences were found between ACE-A and HE-A ($p=0.131$, $p<0.017$) (see Table 4.6).

Differences between Paras and Quads.

Work rate was significantly higher in Paras than Quads for HE-A ($p=0.006$, $p<0.017$) and with ACE-A ($p=0.004$, $p<0.017$)(see Table 4.6), but not with FES-A.

Power Output.

Table 4.7

Training Power Outputs (W) for FES-T, FES-A, ACE-A, and HE-A

Subject#	FES-A	ACE-A	HE-A
1	5.85	5.89	11.74
2	5.85	3.92	9.77
3	0	7.85	7.85
4	0	30.21	25.90
5	8.78	23.54	31.36
6	11.70	23.54	35.28
7	8.78	20.50	21.58
8	8.78	23.54	23.51
Mean	6.22(4.27)	17.37(9.94)	20.87(10.19)
Qmean	5.12(3.68)	9.54(7.48)	12.74(6.11)
Pmean	7.32(5.07)	25.21(3.34)	29.01(5.32)

Note: SD = Standard Deviation. Qmean; Pmean = Mean value for Quads and Paras, QSD; PSD = Standard Deviation for Quads and Paras. Flywheel of FES-LCE measured: 1.606m and travelled 5.965 m/revolution. The flywheel for the ACE measured: 1.00m and travelled 1.430 m/revolution.

Power outputs were significantly higher with ACE-A compared to FES-A ($p=0.016$, $p< 0.017$) and more so with HE-A and FES-A ($p=0.002$, $p<0.017$)(see Table 4.7). No differences were found between ACE-A and HE-A ($p=0.099$, $p<0.017$).

Difference between Quads and Paras.

Power outputs were significantly higher in Paras than Quads during ACE-A ($p=0.009$, $p<0.05$) and during HE-A ($p=0.007$, $p<0.05$). No differences were found during FES-A (see Table 4.7).

Energy Expenditure.

Table 4.8

Subject Caloric Expenditures (Kcal) During an Average Workout at 75% Exercise Intensity

Subject#	FES-A	ACE-A	HE-A
Quads			
1	39.21	63.59	117.19
2	63.59	80.66	125.07
3	90.61	97.44	172.98
7	93.65	129.13	146.26
Mean(SD)	71.77(25.57)	92.71(27.94)	140.38(24.96)
Paras			
4	86.77	158.22	187.36
5	81.66	165.10	206.43
6	122.19	183.81	191.68
8	86.29	118.83	144.29
Mean(SD)	94.23(18.78)	156.49(27.34)	182.44(26.71)
Group Mean	83.00(23.99)	124.60(42.63)	161.41(32.84)

Results showed that ACE-A was significantly higher than FES-A ($p=0.004$, $p< 0.017$), HE-A was significantly higher than ACE-A ($p=0.002$, $p< 0.017$), and HE-A was significantly higher than FES-A ($p=0.000$, $p< 0.017$)(see Table 4.8). As three comparisons were made to determine the difference between FES-A, ACE-A and HE-A the alpha level became 0.017 ($\alpha= 0.05/3$, Bonferroni correction).

Differences between Quads and Paras.

After performing two-tailed t-tests for independent samples to compare Quads and Paras results show that Paras have a higher energy expenditure than Quads when performing ACE-A ($p=0.017$, $p<0.05$), however not with FES-A or HE-A (see Table 4.7).

Correlations

Lipids: Cholesterol levels correlated with LDL levels ($r=0.95$, $p<0.001$). TG levels correlated negatively with HDL and HDL_2 levels throughout the study ($r=-0.75$, $p<0.05$).

Weight: The HDL_2/HDL_3 ratio correlated negatively with weight ($r=-0.70$, $p<0.05$) at FES-A, R_2, R_3, HE-A. HDL_2 correlated negatively with weight ($r=-0.70$, $p<0.05$) for pre-training levels, and FES-A. BMI related to weight ($r=0.76$, $p<0.05$). The maximal aerobic power test for FES-LCE (L/min) correlated with weight throughout the study ($r=0.85$, $p<0.01$). Weight was correlated to average fat consumption (g) prior to training ($r=0.73$, $p=0.05$).

Diet: ACE and FES-LCE maximal aerobic power tests were correlated with average poly/saturated fat in the first dietary record reading. Average poly/saturated fat ratio was also related to HDL and HDL_3 at all levels ($r=0.75$, $p<0.05$ and $r=0.75$, $p<0.05$, respectively). Average fat consumption (g) was related to HDL after FES-T ($r=-0.79$, $p<0.05$), after ACE-A ($r=-0.75$, $p<0.03$), after R_4 ($r=-0.73$, $p<0.05$), and to HDL_2 after ACE-A ($r=-0.80$, $p<0.05$) and after R_4 ($r=-0.77$, $p<0.05$). The HDL_2/HDL_3 ratio was correlated with average fat consumption at the end of the study ($r=-0.72$, $p<0.05$). Calories/weight ratio was correlated with HDL at FES-A ($r=0.74$, $p<0.05$), HDL_2 after FES-A ($r=0.72$, $p<0.05$) and HDL_3 after R_1 ($r=-0.98$, $p<0.005$). Average calories correlated with TC/HDL ratio ($r=-0.80$, $p<0.05$) at baseline and also after FES-T. Average calories at 17 weeks also correlated with ACE-A HDL levels ($r=-0.73$, $p<0.05$).

Table 4.9

HDL Levels over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	1.09	.93	1.09	1.43	1.49	1.2	1.42	1.45	1.16
2	.85	.82	.84	.77	.68	.68	.63	.68	.77
3	1.01	.95	1.05	1.05	.87	.90	.97	1.17	.88
4	1.06	1.18	-	1.05	1.11	1.25	.99	1.27	1.11
5	.73	.66	.90	.90	.91	.88	.96	.91	.95
6	.66	.88	.84	.84	.80	.84	.76	.91	.74
7	.82	1.13	1.03	.92	.98	.95	.90	.85	1.00
8	1.69	1.58	1.39	1.07	1.51	1.55	1.46	1.46	1.43
Mean	.99	1.02	1.02	1.00	1.04	1.03	1.01	1.09	1.00
Quad	.94	.96	1.00	1.04	1.00	.93	.98	1.04	.95
Para	1.03	1.07	1.04	.96	1.08	1.13	1.04	1.14	1.06

Table 4.10

HDL Levels Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	-14.68	17.20	31.19	4.19	-19.46	18.33	2.11	-20.00
2	-3.53	2.44	-8.33	-11.69	0.00	-7.35	7.94	13.23
3	-5.94	10.53	0.00	-17.14	3.45	7.78	20.62	-24.79
4	11.32	-	-	5.71	12.61	-20.8	28.28	-12.60
5	-9.59	36.36	0.00	1.11	-3.30	9.09	-5.21	4.39
6	33.33	-4.54	0.00	-4.76	5.00	-9.52	19.74	-18.68
7	37.80	-8.85	-10.68	6.52	-3.06	-5.26	-5.55	17.65
8	-6.51	-12.02	-23.02	41.12	2.64	-5.81	0.00	-2.05
Mean	2.78	0.37	-1.59	3.98	-1.20	-1.94	7.54	-7.59
Quad	1.59	4.70	3.99	-3.60	-7.21	5.09	5.87	-8.19
Para	3.86	-2.94	-7.51	12.18	4.39	-7.74	9.11	-7.03

Table 4.11

HDL Levels Relative to Baseline Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	-14.68	0	31.19	36.70	10.09	30.27	33.03	6.42
2	-3.53	-1.17	-9.41	-20.00	-20.00	-25.88	-20.00	-9.41
3	-5.94	3.96	3.96	-13.86	-10.89	-3.96	15.84	-12.87
4	11.32	-	-0.94	4.72	17.92	-6.60	19.81	4.72
5	-9.59	23.29	23.29	24.66	20.55	31.51	24.66	30.14
6	33.33	27.27	27.27	21.21	27.27	15.15	37.88	12.12
7	37.80	25.61	12.19	19.51	15.85	9.76	3.65	21.95
8	-6.51	-17.75	-36.69	-10.65	-8.28	-13.61	-13.61	-15.38
Mean	2.78	3.16	1.52	5.56	4.30	2.27	9.99	1.64
Quad	1.59	6.37	10.61	6.63	-1.06	3.98	10.08	1.06
Para	3.86	0.80	-6.76	4.59	9.18	0.72	9.90	2.17

Table 4.12

HDL_2 Levels Over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	.22	.25	-	.56	.56	.37	.52	.60	.33
2	.09	.12	-	.09	-	.04	.00	.09	.09
3	.12	.15	.11	.09	.01	.08	.11	.24	.09
4	.30	.19	-	.28	.29	.43	.25	.37	.37
5	.05	.08	.17	.11	.14	.13	.27	.21	.25
6	.10	-	.00	.06	.15	.05	.05	.08	.05
7	.14	.15	.09	.07	.08	.03	.09	.08	.17
8	.63	.67	.51	.42	.49	.56	.48	.56	.50
Mean	.21	.23	.18	.21	.24	.21	.22	.28	.23
Quad	.14	.17	.10	.20	.22	.13	.18	.25	.17
Para	.27	.31	.23	.22	.27	.29	.26	.30	.29

Table 4.13

HDL_2 Levels Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	13.64	-	-	0.00	-33.93	40.54	15.38	-45.00
2	33.33	-	-	-	-	-100.00	-	0.00
3	25.00	-26.67	-18.18	-88.89	700.00	37.50	118.18	-62.50
4	-36.67	-	-	3.57	48.28	-41.86	48.00	0.00
5	60.00	112.5	-35.29	27.27	-7.14	107.69	-22.22	19.05
6	-	-	-	150.00	-66.67	0.00	60.00	-37.50
7	7.14	-40.00	-22.22	14.28	-62.50	200.00	-11.11	112.50
8	6.35	-23.88	-17.65	16.67	14.29	-14.29	16.67	-10.71
Mean	11.51	-23.48	19.32	17.01	-14.03	4.73	25.99	-17.04
Quad	17.54	-33.33	102.50	7.00	-40.00	38.46	40.28	-32.67
Para	16.05	44.31	-26.47	22.99	9.35	-10.26	16.19	-4.10

Table 4.14

HDL_2 Levels Relative to Baseline Expressed as Percent Change

	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	13.64	-	154.54	154.54	68.18	136.36	172.72	50.00
2	33.33	-	0.00	-	-55.56	-100.00	0.00	0.00
3	25.00	-8.33	-25.00	-91.67	-33.33	-8.33	100.00	-25.00
4	-36.67	-	-6.67	-3.33	43.33	-16.67	23.33	23.33
5	60.00	240.00	120.00	180.00	160.00	440.00	320.00	400.00
6	-	-100.00	-40.00	50.00	-50.00	-50.00	-20.00	-50.00
7	7.14	-35.71	-50.00	-42.86	-78.57	-35.71	-42.86	21.43
8	6.35	-19.05	-33.33	-22.22	-11.11	-23.81	-11.11	-20.63
Mean	11.51	-14.67	1.82	19.13	2.42	7.27	35.15	12.12
Quad	17.54	-29.82	42.10	52.05	-8.77	26.31	77.19	19.30
Para	16.05	-16.05	-19.44	-0.93	8.33	-2.78	12.96	8.33

Table 4.15

HDL_3 Levels over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	.87	.68	-	.84	.93	.83	.90	.85	.83
2	.76	.70	-	.68	.68	.64	.64	.59	.68
3	.89	.80	.94	.96	.86	.82	.85	.93	.79
4	.76	.99	-	.77	.82	.82	.74	.90	.74
5	.60	.58	.73	.79	.77	.75	.69	.70	.70
6	.62	-	.86	.77	.65	.79	.74	.83	.69
7	.62	.98	.94	.85	.90	.92	.81	.77	.83
8	.92	.91	.88	.65	1.02	.99	.98	.90	.93
Mean	.75	.81	.87	.79	.83	.82	.79	.81	.77
Quad	.78	.79	.94	.83	.84	.80	.80	.78	.78
Para	.72	.83	.82	.74	.81	.84	.79	.83	.76

Table 4.16

HDL_3 Levels Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	-21.84	-	-	10.71	-10.75	8.43	-5.55	-2.35
2	-7.89	-	-	0.00	-5.88	0.00	-7.81	15.25
3	-10.11	17.5	2.13	-10.42	-4.65	3.66	9.41	-15.05
4	30.26	-	-	6.49	0.00	-9.76	21.62	-17.78
5	-3.33	25.86	8.22	-2.53	-2.60	-8.00	1.45	0.00
6	-	-	-10.46	-15.58	21.54	-6.33	12.16	-16.87
7	58.06	-4.08	-9.57	5.88	2.22	-11.96	-4.94	7.79
8	-1.09	-3.30	-26.14	56.92	-2.94	-1.01	-8.16	3.33
Mean	6.72	7.98	-9.34	5.07	-1.05	-3.20	1.89	-4.33
Quad	0.64	18.99	-11.44	1.20	-4.75	-0.31	-1.87	-0.32
Para	14.02	-0.40	-9.51	9.39	2.76	-5.97	5.71	-8.11

Table 4.17

HDL_3 Levels Relative to Baseline Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	-21.84	-	-3.45	6.90	-4.60	3.45	-2.30	-4.60
2	-7.89	-	-10.53	-10.53	-15.79	-15.79	-22.37	-10.53
3	-10.11	5.62	7.86	-3.37	-7.86	-4.49	4.49	-11.24
4	30.26	-	1.32	7.89	7.89	-2.63	18.42	-2.63
5	-3.33	21.67	31.67	28.33	25.00	15.00	16.67	16.67
6	-	38.71	24.19	4.84	27.42	19.35	33.87	11.29
7	58.06	51.61	37.10	45.16	48.39	30.64	24.19	33.87
8	-1.09	-4.35	-29.35	10.86	7.61	6.52	-2.17	1.09
Mean	6.72	15.23	4.47	9.77	8.61	5.13	7.12	2.48
Quad	0.64	19.74	6.05	7.32	2.23	1.91	0.00	-0.32
Para	14.02	13.56	2.76	12.41	15.52	8.62	14.83	5.52

Table 4.18

TC/HDL Ratio Over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	3.82	5.11	4.41	3.43	3.65	4.15	3.51	3.42	4.33
2	4.73	4.27	4.18	4.01	4.62	5.26	5.19	4.65	4.26
3	6.70	5.96	6.19	5.74	6.79	6.64	6.28	5.71	7.08
4	4.32	3.97	-	4.83	4.73	4.13	4.47	4.12	4.74
5	4.27	4.86	3.93	4.16	3.83	4.03	3.91	4.63	3.70
6	7.02	5.85	6.80	6.21	6.80	6.32	6.84	6.15	6.46
7	3.84	3.95	4.28	4.81	4.32	4.74	4.41	4.59	4.27
8	3.30	3.77	4.87	5.15	3.79	3.48	3.97	3.73	4.15
Mean	4.75	4.72	4.95	4.79	4.82	4.84	4.82	4.62	4.87
Quad	4.77	4.82	4.76	4.50	4.84	5.20	4.85	4.59	4.98
Para	4.73	4.61	5.20	5.09	4.79	4.49	4.80	4.66	4.76

Table 4.19

TC/HDL Ratio Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	33.77	-13.70	-22.22	6.41	13.70	-15.42	-2.56	26.61
2	-9.72	-2.11	-4.07	15.21	13.85	-1.33	-10.40	-8.39
3	-11.04	3.86	-7.27	18.29	-2.21	-5.42	-9.08	23.99
4	-8.10	-	-	-2.07	-12.68	8.23	-7.83	15.05
5	13.82	-19.14	5.85	-7.93	5.22	-2.98	18.41	-20.09
6	-16.67	16.24	-8.68	9.50	-7.06	8.23	-10.09	5.04
7	2.86	8.35	12.38	-10.19	9.72	-6.96	4.08	-6.97
8	14.24	29.18	5.75	-26.41	-8.18	14.08	-6.04	11.26
Mean	-0.68	4.96	-3.21	0.49	0.57	-0.44	-4.09	5.38
Quad	1.05	-1.19	-5.61	7.73	7.27	-6.73	-5.26	8.55
Para	-2.43	12.74	-2.16	-5.90	-6.21	6.85	-2.92	2.25

Table 4.20

TC/HDL Ratio Relative to Baseline Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	33.77	15.44	-10.21	-4.45	8.64	-8.11	-10.47	13.35
2	-9.72	-11.63	-15.22	-2.32	11.20	9.72	-1.69	-9.94
3	-11.04	-7.61	-14.33	1.34	-0.89	-6.27	-14.78	5.67
4	-8.10	-	11.80	9.49	-4.40	3.47	-4.63	9.72
5	13.82	-7.96	-2.58	-10.30	-5.62	-8.43	8.43	-13.35
6	-16.67	-3.13	-11.54	-3.13	-9.97	-2.56	-12.39	-7.98
7	2.86	11.46	25.26	12.50	23.44	14.84	19.53	11.20
8	14.24	47.57	56.06	15.85	5.45	20.30	13.03	25.76
Mean	-0.68	4.24	0.89	1.39	1.97	1.53	-2.63	2.60
Quad	1.05	-0.16	-5.76	1.52	8.90	1.57	-3.77	4.45
Para	-2.43	9.99	7.61	1.27	-5.02	1.48	-1.48	0.74

Table 4.21

HDL_2/HDL_3 Ratio Over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	.25	.37	-	.64	.60	.45	.58	.71	.40
2	.12	.17	-	.13	.00	.06	.00	.15	.13
3	.13	.19	.12	.09	.01	.10	.13	.26	.11
4	.39	.19	-	.36	.35	.52	.34	.41	.50
5	.08	.14	.23	.14	.18	.17	.39	.30	.36
6	.16	-	.00	.08	.23	.06	.07	.10	.07
7	.23	.15	.10	.08	.09	.03	.11	.10	.20
8	.68	.74	.58	.65	.48	.57	.49	.62	.54
Mean	.25	.28	.21	.27	.24	.24	.26	.33	.29
Quad	.18	.22	.11	.23	.17	.16	.20	.31	.21
Para	.33	.36	.27	.31	.31	.33	.32	.36	.37

Table 4.22

HDL_2/HDL_3 Ratio Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	48.00	-	-	-6.25	-25.00	28.89	22.41	-43.66
2	41.67	-	-	-100.00	-	-100.00	-	-18.75
3	46.15	-36.84	-25.00	-88.89	900.00	30.00	100.00	-57.69
4	-51.28	-	-	-2.78	48.57	-34.61	20.59	21.95
5	75.00	64.28	-39.13	28.57	-5.55	129.41	-23.08	20.00
6	-	-	-	187.50	-73.91	16.67	42.86	-30.00
7	-34.78	-33.33	-20.00	12.50	-66.67	266.67	-9.09	100.00
8	8.82	-21.62	12.07	-26.15	18.75	-14.03	26.53	-12.90
Mean	9.24	-26.05	31.67	-10.60	11.93	-2.83	26.07	-13.16
Quad	20.55	-50.00	113.64	-25.53	-8.57	28.12	50.00	-31.71
Para	8.91	-24.30	13.89	0.81	35.48	-23.21	10.85	2.80

Table 4.23

HDL_2/HDL_3 Ratio Relative to Baseline Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	48.00	-	156.00	140.00	80.00	132.00	184.00	60.00
2	41.67	-	8.33	-100.00	-50.00	-100.00	33.33	8.33
3	46.15	-7.69	-30.77	-92.31	-23.08	0.00	100.00	-15.38
4	-51.28	-	-7.69	-10.26	33.33	-12.82	5.13	28.20
5	75.00	187.50	75.00	125.00	112.50	387.50	275.00	350.00
6	-	-100.00	-50.00	43.75	-62.50	-56.25	-37.50	-56.25
7	-34.78	-56.52	-65.21	-60.87	-86.96	-52.17	-56.52	-13.04
8	8.82	-14.52	-4.41	-29.41	-16.18	-27.94	-8.82	-20.59
Mean	9.24	-19.21	6.37	-4.90	6.44	3.43	30.39	13.23
Quad	20.55	-39.73	28.77	-4.11	-12.33	12.33	68.49	15.07
Para	8.91	-17.56	-6.11	-5.34	28.24	-1.53	9.16	12.21

Table 4.24

LDL Levels Over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	3.43	3.66	3.50	3.37	3.82	3.68	3.39	3.40	3.72
2	2.43	2.32	2.36	2.06	2.28	2.66	2.38	2.02	2.20
3	4.38	4.36	5.09	4.66	4.65	4.76	4.79	5.12	4.87
4	3.2	3.30	-	3.78	3.87	3.69	3.16	3.78	3.81
5	2.41	2.34	2.39	2.62	2.24	2.34	2.47	2.89	2.27
6	2.94	3.36	4.51	3.94	3.96	3.99	3.98	4.44	3.47
7	2.75	3.04	3.10	3.26	2.97	3.23	2.87	2.81	2.91
8	3.39	4.2	4.41	3.92	3.90	3.56	4.07	3.73	4.31
Mean	3.12	3.32	3.62	3.45	3.46	3.49	3.39	3.52	3.44
Quad	3.25	3.34	3.51	3.34	3.43	3.58	3.36	3.34	3.43
Para	2.98	3.30	3.77	3.56	3.49	3.39	3.42	3.71	3.46

Table 4.25

LDL Levels Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	6.70	-4.37	-3.71	13.35	-3.66	-7.88	0.35	9.35
2	-4.53	1.72	-12.71	10.68	16.67	-10.53	-15.21	9.11
3	-0.46	16.74	-8.45	-0.21	2.36	0.63	6.85	-4.84
4	3.12	-	-	2.38	-4.65	-14.36	19.62	0.69
5	-2.90	2.14	9.62	-14.50	4.46	5.55	17.08	-21.37
6	14.29	34.23	-12.64	0.51	0.76	-0.25	11.51	-21.86
7	10.54	1.97	5.16	-8.90	8.75	-11.14	-2.02	3.63
8	23.89	5.00	-11.11	-0.51	-8.71	14.33	-8.40	15.66
Mean	6.61	9.04	-4.74	0.29	0.79	-2.87	3.98	-2.20
Quad	3.00	5.01	-4.98	2.77	4.45	-6.28	-0.60	2.67
Para	10.55	14.24	-5.44	-2.03	-2.79	0.74	8.46	-6.59

Table 4.26

LDL Levels Relative to Baseline Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	6.70	2.04	-1.75	11.37	7.29	-1.17	-0.82	8.45
2	-4.53	-2.88	-15.23	-6.17	9.46	-2.06	-16.95	-9.38
3	-0.46	16.21	6.39	6.16	8.67	9.36	16.85	11.19
4	3.12	-	18.12	20.94	15.31	-1.25	18.12	18.94
5	-2.90	-0.83	8.71	-7.05	-2.90	2.49	20.00	-5.64
6	14.29	53.40	34.01	34.69	35.71	35.37	50.95	17.96
7	10.54	12.73	18.54	8.00	17.45	4.36	2.25	5.96
8	23.89	30.09	15.63	15.04	5.01	20.06	9.97	27.20
Mean	6.62	16.26	10.75	11.07	11.95	8.74	13.07	10.57
Quad	3.00	8.16	2.77	5.62	10.31	3.39	2.77	5.51
Para	10.55	26.30	19.43	17.00	13.73	14.57	24.27	16.08

Table 4.27

TG Levels Over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	0.72	0.78	1.08	0.54	0.63	0.51	0.90	0.54	0.70
2	2.82	1.78	1.57	1.31	0.89	1.18	1.31	2.31	1.54
3	2.02	1.77	1.80	1.58	1.93	1.61	1.64	1.96	2.40
4	1.80	1.00	-	1.20	1.37	1.10	1.41	0.90	1.72
5	1.55	1.05	1.25	1.10	1.68	1.63	1.58	2.04	1.48
6	2.52	2.00	1.82	2.18	3.42	2.38	2.32	1.26	2.86
7	1.10	1.46	1.40	1.27	1.39	1.60	1.02	1.19	1.78
8	2.02	0.89	0.81	2.60	1.62	1.42	1.34	1.31	0.99
Mean	1.82	1.34	1.39	1.47	1.62	1.43	1.44	1.44	1.68
Quad	1.66	1.45	1.46	1.17	1.21	1.22	1.22	1.50	1.60
Para	1.97	1.23	1.29	1.77	2.02	1.63	1.66	1.38	1.76

Table 4.28

TG Levels Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	8.33	38.46	-50.00	16.67	-19.05	76.47	-40.00	29.63
2	-36.88	-11.80	-16.56	-32.06	32.58	11.01	76.33	-33.33
3	-12.38	1.69	-12.22	22.15	-16.58	1.86	19.51	22.45
4	-44.44	-	-	14.17	-19.71	28.18	-36.17	91.11
5	-32.26	19.05	-12.00	52.73	-2.98	-3.07	29.11	-27.45
6	-20.63	-9.00	19.78	56.88	-30.41	-2.52	-45.69	126.98
7	32.73	-4.11	-9.28	9.45	15.11	-36.25	16.67	49.58
8	-55.94	-8.99	220.99	-37.69	-12.34	-5.63	-2.24	-24.43
Mean	-26.25	3.63	5.93	9.76	-11.60	0.79	-0.09	17.03
Quad	-13.06	1.04	-19.66	2.98	1.24	-0.61	23.20	7.00
Para	-37.39	4.72	36.86	14.26	-19.28	1.84	-17.14	27.95

Table 4.29

TG Levels Relative to Baseline Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	8.33	50.00	-25.00	-12.50	-29.17	25.00	-25.00	-2.78
2	-36.88	-44.33	-53.55	-68.44	-58.16	-53.55	-18.08	-45.39
3	-12.38	-10.89	-21.78	-4.45	-20.30	-18.81	-2.97	18.81
4	-44.44	-	-33.33	-23.89	-38.89	-21.67	-50.00	-4.44
5	-32.26	-19.35	-29.03	8.39	5.16	1.93	31.61	-4.52
6	-20.63	-27.78	-13.49	35.71	-5.55	-7.94	-50.00	13.49
7	32.73	27.27	15.45	26.36	45.45	-7.27	8.18	61.82
8	-55.94	-59.90	28.71	-19.80	-29.70	-33.66	-35.15	-50.99
Mean	-26.25	-23.57	-19.04	-11.13	-21.44	-20.82	-20.89	-7.42
Quad	-13.06	-12.16	-29.43	-27.33	-26.43	-26.88	-9.91	-3.60
Para	-37.39	-34.43	-10.27	2.53	-17.24	-15.72	-30.16	-10.65

Table 4.30

TC Levels Over Time (mmol/L)

Subject #	Baseline	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	4.66	4.75	4.81	4.91	5.44	4.98	4.99	4.96	5.02
2	3.84	3.50	3.51	3.09	3.14	3.58	3.27	3.16	3.28
3	5.79	5.66	6.50	6.03	5.91	5.98	6.09	6.68	6.23
4	4.62	4.68	-	5.07	5.25	5.16	4.43	5.23	5.26
5	3.45	3.21	3.54	3.74	3.49	3.55	3.75	4.21	3.52
6	4.10	5.15	5.71	5.22	5.44	5.31	5.20	5.60	4.78
7	3.79	4.46	4.41	4.43	4.23	4.50	3.97	3.90	4.27
8	5.48	5.96	5.96	5.51	5.73	5.39	5.80	5.45	5.94
Mean	4.47	4.67	4.92	4.75	4.83	4.81	4.69	4.90	4.79
Quad	4.52	4.59	4.81	4.61	4.68	4.76	4.58	4.67	4.70
Para	4.41	4.75	5.07	4.88	4.98	4.85	4.79	5.12	4.87

Table 4.31

TC Relative to Rest Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	1.93	1.26	2.08	10.79	-8.45	0.20	-0.60	1.21
2	-8.85	0.29	-11.97	1.62	14.01	-8.66	-3.36	3.80
3	-2.24	14.84	-7.23	-1.99	1.18	1.84	9.69	-6.74
4	1.30	-	-	3.55	-1.71	-14.15	18.06	0.57
5	-6.96	10.28	5.65	-6.68	1.72	5.63	12.27	-16.39
6	25.61	10.87	-8.58	4.21	-2.39	-2.07	7.69	-14.64
7	17.68	-1.12	0.45	-4.51	6.38	-11.78	-1.76	9.49
8	8.76	0.00	-7.55	3.99	-5.93	7.61	-6.03	8.99
Mean	4.59	5.32	-3.45	1.66	-0.47	-2.47	4.51	-2.27
Quad	1.60	4.68	-4.00	1.41	1.71	-3.78	2.07	0.53
Para	7.65	6.74	-3.65	1.89	-2.51	-1.18	6.83	-4.83

Table 4.32

TC Levels Relative to Baseline Expressed as Percent Change (%)

Subject #	FES-T	R_1	FES-A	R_2	ACE-A	R_3	HE-A	R_4
1	1.93	3.22	5.36	16.74	6.87	7.08	6.44	7.72
2	-8.85	-8.59	-19.53	-18.23	-6.77	-14.84	-17.71	-14.58
3	-2.24	12.26	4.14	2.07	3.28	5.18	15.37	7.60
4	1.30	- -	9.74	13.64	11.69	-4.11	13.20	13.85
5	-6.96	2.61	8.40	1.16	2.90	8.70	22.03	2.03
6	25.61	39.27	27.32	32.68	29.51	26.83	36.58	16.58
7	17.68	16.36	16.89	11.61	18.73	4.75	2.90	12.66
8	8.76	8.76	0.55	4.56	-1.64	5.84	-0.55	8.39
Mean	4.59	10.16	6.35	1.66	8.12	7.61	9.68	7.19
Quad	1.60	6.36	2.10	3.54	5.31	1.33	3.43	3.98
Para	7.65	14.90	10.71	12.80	9.97	8.67	16.09	10.48

Table 4.33

Dietary Variables in First, Second, and Third Dietary Record

Sub#	calories			protein			carbohydrates			fat (%)			fat (grams)			poly/sat ratio		
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
1	1846	2072	2033	74.8	65.6	65.7	230	229	210	28	29	34	57.2	65.4	72.9	0.9	0.4	0.8
2	1708	1223	1918	61.9	56.9	51.8	233	163	250	21	28	27	47.9	39.9	65.3	0.6	0.4	0.3
3	2356	1338	1974	81.2	52.6	92.0	190	148	180	53	42	45	144.0	62.3	99.8	0.7	0.7	0.8
4	1647	1821	1830	61.3	83.9	62.2	249	237	289	23	23	19	44.1	48.5	44.4	0.3	0.7	1.0
5	2065	1674	2307	58.6	57.0	199.7	255	168	207	29	39	38	73.9	75.5	93.6	0.6	0.4	0.6
6	3487	1460	1943	178.3	52.0	62.4	447	189	237	29	33	39	111.7	58.9	85.7	0.5	0.1	0.8
7	2041	1482	1953	89.6	53.1	73.4	190	161	199	33	26	33	75.4	47.3	76.3	0.3	0.6	0.9
8	1225	1067	1151	39.3	43.3	38.0	192	178	199	29	19	22	39.6	25.9	27.6	0.6	0.9	0.6
Mean	2047	1517	1889	80.6	58.1	70.6	248	184	221	31	30	32	74.2	53.0	70.7	0.6	0.5	0.7
SD	672	327	329	42.4	12.2	25.2	85	32	35	10	8	9	36.6	15.8	24.5	0.2	0.3	0.2

Note: 1,2, 3 correspond to dietary records completed at baseline, after FES-T, and after HE-A.

Table 4.34

Weight and Calories/Weight Ratio Over Time

Subject #	Weight (kg)					Calories/weight ratio		
	Baseline	FES-T	FES-A	ACE-A	HE-A	1	2	3
1	56.1	55.8	55.5	55.5	55.4	32.9	37.1	36.7
2	75.0	76.3	76.1	75.8	78.2	22.7	16.0	24.5
3	113.7	107.3	107.0	107.0	110.0	20.7	12.5	17.9
4	74.2	73.3	74.6	74.3	74.3	22.2	24.9	24.6
5	77.9	74.8	74.9	73.9	72.7	26.5	22.4	31.7
6	98.0	98.0	100.5	97.4	97.3	35.6	14.9	20.0
7	115.0	115.0	117.0	120.0	125.8	17.8	12.9	15.5
8	76.1	72.8	72.4	70.3	70.9	16.1	14.7	16.2
Mean	85.8	84.1	84.7	84.3	85.6	24.3	19.4	23.4
SD	20.9	20.3	20.9	21.6	23.4	6.9	8.5	8.2

Note: 1,2, and 3 correspond to dietary records completed at baseline, after FES-T, and after HE-A.

CHAPTER 5
DISCUSSION

Subjects

Eight self-selected subjects participated in this study. The reason eight subjects - and not more - were involved in the study, was due to the fact that only eight subjects out of the 12 who underwent medical examination were eligible to participate. Those who were excluded did not have a lower motor neuron lesion and did not respond to stimulation. However, a small sample size is not uncommon in research dealing with people with SCI, as Hooker et al. (1992) and Hooker, Scremin, Mutton, Kunkel, & Cagle, (1995) also used eight subjects. As a consequence, results were limited to the subjects who participated in the study and may not be generalized to other individuals with SCI.

Lipid levels: Group Analysis

No significant changes were found in lipid-lipoprotein profile when pre- and post blood samples were compared. In addition, no significant differences were found between Quads and Paras.

In relation to other research, baseline HDL levels in this study were higher (0.99 ± 0.34 mmol/L) than those found in other sedentary subjects (0.88 mmol/L) (Dearwater et al., 1986; Brenes et al., 1986), (0.95 mmol/L) (Dallmeijer et al., 1997) and higher than the 0.91 mmol/L value associated with increased risk of CVD. HDL levels were similar to those found by Maki et al. (1995) (1.00 mmol/L) and lower than those reported for the same age group (1.12 mmol/L) by Krum et al. (1992). The reason for higher HDL levels in this subject sample was attributed to the female participant in the study which undoubtably raised the average HDL level. The higher HDL levels may also be due to the fac that all subjects were employed and perhaps not as sedentary as unemployed persons.

Some studies have separated Quads and Paras into two groups or have simply investigated one group. In the present study, HDL levels were higher in Paras than Quads (1.03 vs. 0.94 mmol/L) however this did not reach significance. Similar values in Paras

were found by Janssen et al., (1997) (1.05 mmol/L), while higher values were found by Bostom et al., (1991) (1.18 mmol/L). Lower values have been identified by Bauman et al. (1992b) (0.95 mmol/L) and by Bauman et al. (1992a) (0.93 mmol/L). Some authors have found no differences between Quads and Paras (Brenes et al., 1986; Cardús et al., 1992; Janssen et al., 1997; Maki et al., 1995) however, there was likely a relationship between HDL values and exercise participation. Brenes et al. (1986) demonstrated that athletes with SCI had higher HDL levels (1.09 mmol/L) than persons who were sedentary and Dallmeijer et al. (1997) found that sport activity was the only determinant of HDL. Therefore, due to the correlation between HDL levels and physical activity it is possible to assume that Paras with lower lesion levels and more movement above the waist would be more physically active than Quads. Increased mobility and upper body strength appeared to separate the Paras and the Quads in this study perhaps also accounting for the increased HDL levels.

Baseline HDL_2 levels in this study were similar to those found by Dearwater et al. (1986) (0.21 mmol/L vs. 0.23 mmol/L, respectively). Higher levels were found by Shetty et al. (1992) (0.32 mmol/L) while lower levels were found by Janssen et al. (1997) (0.15 mmol/L).

Baseline HDL_3 levels were higher in this study (0.76 ± 0.13 mmol/L) compared to those reported by Dearwater et al. (1986)(0.65 mmol/L) and lower compared to those in Janssen et al. (1997) (0.90 mmol/L). However, subjects in Janssen et al. were young (37.4 years), healthy, and active, and were not representative of the population in this study. Increases in HDL_3 mass account for changes in HDL particle mass (Dearwater et al., 1986). Brenes et al. (1989) have also observed a nonsignificant increase in HDL mass accompanied by a significant increase in HDL_3 (0.71 vs .80 mmol/L) and a slight insignificant decrease in HDL_2 after performing 47 sessions of FES-LCE. The nonsignificant change in HDL_2 were attributed to a relatively low intensity training program (Brenes et al., 1989). However, these conclusions were obtained from a subject sample of five, three Quads and two Paras. Also, there were two females who may have been responsible for the increased average HDL levels (1.11 mmol/L) found by this study.

To date, the absence of values for HDL_2 and HDL_3 associated with CVD made it difficult to conclude which was more protective. However, relative to published research, it appeared that this subject sample had average values.

The mean TC/HDL ratio at baseline in the present study was lower than those reported by the literature. The ratio was similar in Quads and Paras. In this study the 4.75 value was lower than the 5.45 value in Quads reported by Shetty et al. (1992), 5.30 value in Quads in Dallmeijer et al. (1997), 5.04 value in Quads and Paras reported by Maki et al. (1995), 4.98 value for active Quads and Paras observed in Janssen et al. (1997), and the 5.50 value in Paras and 4.90 value in Quads measured in Bauman et al. (1992). The only study which reported a lower ratio (4.29 value) was Bostom et al. (1991) who investigated lipid-lipoprotein profiles and VO_2 in independently living Paras. The reason for decreased TC/HDL ratios compared to other published results was that this group had lower TC levels and higher HDL levels. Therefore, subjects in this study were at low CVD risk and had levels similar to active individuals.

Baseline LDL levels reported by this present study (3.12 mmol/L) were lower than those reported by Janssen et al. (1997) (3.21 mmol/L) and similar to those reported by Maki et al. (1995) (3.12 mmol/L). LDL levels observed in Quads were higher (3.25 mmol/L) than those reported by Janssen et al. (1997) (3.15 mmol/L) and those by Shetty et al. (1992) (3.01 mmol/L). However, levels were lower than those found by Bauman et al. (1992) (3.28 mmol/L) and Dallmeijer et al. (1997)(3.4 mmol/L). Paras LDL levels were lower than those reported by Janssen et al. (1997) (2.98 vs. 3.28 mmol/L) and those reported by Bauman et al. (1992) (3.17 mmol/L). Overall, subjects were found to be below CVD risk levels (3.40mmol/L) and were similar to other reported findings. Interestingly, Quads had higher or similar values and Paras had lower values than other research.

Baseline TG values in this study were measured in subjects who underwent a 12 hour overnight fast. As some studies have not required subjects to fast, comparisons in TG levels among studies were limited. Janssen et al. (1997), Dearwater et al. (1986) and Maki et al. (1995) reported lower values (1.64 mmol/L, 1.50 mmol/L, and 1.56 mmol/L, respectively) than those measured in this study (1.82 mmol/L). TG values in both Quads

and Paras (1.66 mmol/L and 1.97 mmol/L, respectively) were higher than those reported (1.41 mmol/L and 1.84 mmol/L, respectively) by Janssen et al. (1997). Therefore, it appeared that TG levels in this study were higher than other reported findings. Higher TG levels suggested decreased degradation of TG containing molecules in the circulation commonly observed in persons with insulin-resistance and/or decreased LPL.

Group TC levels in this study were lower (4.47 mmol/L) than those reported by Maki et al. (1995) (4.76 mmol/L), and Janssen et al. (1997) (5.12 mmol/L). TC levels were similar to those observed in sedentary SCI (Quads: 4.52 vs. 4.47 mmol/L; Paras: 4.41 vs. 4.41 mmol/L) (Brenes et al., 1986). TC levels in Quads were lower than the 5.02 value in Shetty et al. (1992). TC levels in Paras were lower than 5.24 mmol/L reported by Bostom et al. (1991) and lower than 4.96 mmol/L by Bauman et al. (1992a). Therefore, TC levels in this study were similar or lower to reported findings in this area. Notable to mention is that TC levels are usually normal in the SCI population which conceals low HDL levels thus making TC a fallacious predictor of CVD risk.

Lipid Levels with Training

After calculating percent change relative to baseline for the group, HDL, HDL_2, and HDL_2/HDL_3 all increased to a greater extent with HE-A than with ACE-A, FES-A, and FES-T (See Figure 4.1), however the changes were not statistically significant. LDL and TC increased, and TG decreased with all interventions, however this did not reach statistical significance (see Figure 4.2). These findings will be discussed in the following text.

To determine what the sample size should have been in order to reach statistical significance ($\alpha \leq 0.05$) at a desired power of 0.80, the following formula was employed (Cohen, 1969):

$$n = \frac{n_{.05}}{400f^2} + 1$$

where $n_{.05}$ is the necessary sample size for the given significance level, degrees of freedom (df), and desired power at the effect size (f)= 0.05, which is found in sample size tables (Cohen, 1969), and f is the nontabled effect size. Given this formula the following table has been developed.

Table 5.1

Calculated Sample Size at Power = 0.80, $\alpha = 0.05$, and df = 4 for Lipid and Lipoprotein Variables

Variables	$n_{.05}$	f	n
HDL	956	0.068	518
HDL_2	956	0.147	112
HDL_3	956	0.033	2, 194
LDL	956	0.270	34
TG	956	0.176	78
TC	956	0.217	52

In this study, large increases in HDL levels (large effect size) were anticipated due to initially low baseline levels. Therefore, HDL levels were expected to significantly increase despite the small subject sample. However, results show that subjects did not all consistently increase HDL levels and in fact three subjects decreased below baseline levels. Thus a larger sample size (n=518) or possibly a longer training period (> one week) would have been necessary for HDL levels to significantly increase.

Group Analysis with Percent Change

Although no statistical changes were found in the group, individual lipid changes did occur. The lack of statistical change may have been due to a large inter subject variability. Some subjects were obese while others were not, some subjects were Quads

while others were Paras, some people ate restaurant food as part of their regular diet while others ate at home, and some people lost weight during the study while others gained weight. All of these factors influenced lipid levels. The most common observation was that rest levels were somewhat elevated or depressed after performing interventions, rarely returning to baseline. Therefore, pre-post or rest-exercise differences were not apparent. One could speculate that one week of rest was not enough time for levels to return to baseline. However, more than one week of rest may have also caused exercise performance to decrease substantially.

Results based on percent change demonstrate that there were increases in HDL, HDL_2 and HDL_2/HDL_3. The most noticeable changes were noted after HE-A. Research states that HDL levels are affected by increased VLDL degradation (Tikannen et al., 1996), LPL (Després & Lamarche, 1994), exercise intensity (Hooker & Wells, 1989; Stein et al., 1990), blood flow (Ruys et al., 1989), muscle fibre type (Andersen et al., 1996), consumption of saturated fats (Fernandez et al., 1995), and weight loss (William et al., 1990).

Increased VLDL degradation would result from increased catabolism of TG-rich lipoproteins which results in the formation of HDL_2 (Després & Lamarche, 1994; Nestel, 1987). As HDL_2 levels increased in this study, results agree with prior research. Increased catabolism of TG-rich particles was thought to be attributed to increased LPL activity at skeletal muscle as a result of increased FFA uptake. Increased action of LPL would 1) increase VLDL/chylomicron remnants for HDL_3 formation, and 2) increase HDL cholesterol via increased CETP action (Tikannen et al., 1996). As HDL_3 particles accumulate cholesterol and get larger, they are transformed into HDL_2 by the action of LCAT. In turn, HDL_2, through the action of HL, is catabolized to form nascent HDL_3 particles (ibid.). Although HDL_2 is correlated with decreased risk of CVD due to its longer half-life in the circulation and larger particle size, an increase in HDL_3 is also beneficial as HDL_3 increase the potential for cholesterol clearance from tissues.

As HDL_3 levels increased in this study, it was speculated that HL increased, however the rise in HDL_2/HDL_3 ratio suggests that there was a higher LPL activity relative to HL activity. This increased LPL to HL activity has been reported to occur with

endurance training (Després & Lamarche, 1994).

The rise in HDL may have occurred to the greatest extent with HE-A as it was the last treatment and would have given muscles enough time to increase capillary density, oxidative capacity and insulin sensitivity (Buemann & Tremblay, 1996). As HE, which incorporates FES-LCE and ACE, has also been shown to increase blood flow (Phillips et al., 1995) and MHC Type I and Type IIa fibres (Andersen et al., 1996), it is possible that these physiological adaptations could have also been responsible for the increase in HDL levels. These changes would have influenced the potential to increase the percentage of total muscle mass available to perform work at a higher exercise intensity, and perhaps also blood flow to the oxygen using muscles. Research has shown that increases in blood flow to muscle can increase HDL_2 and HDL_3 due a greater delivery of substrate (chylomicrons and VLDL) to LPL which is bound to muscle (Ruys et al., 1989).

Another reason for the increase in HDL_2 and HDL_3 may have been attributed to individual high fat diets for increases in calories, particularly those from saturated fats, have been reported to increase HDL (Gidez & Eder, 1984; Fernandez et al., 1995). The mechanism for this action begins with increased VLDL production in the blood as result of increased fat intake, increased catabolism through LPL action, increased muscle uptake of FFA, and increased transfer of surface components to subsequently increase HDL_2 levels.

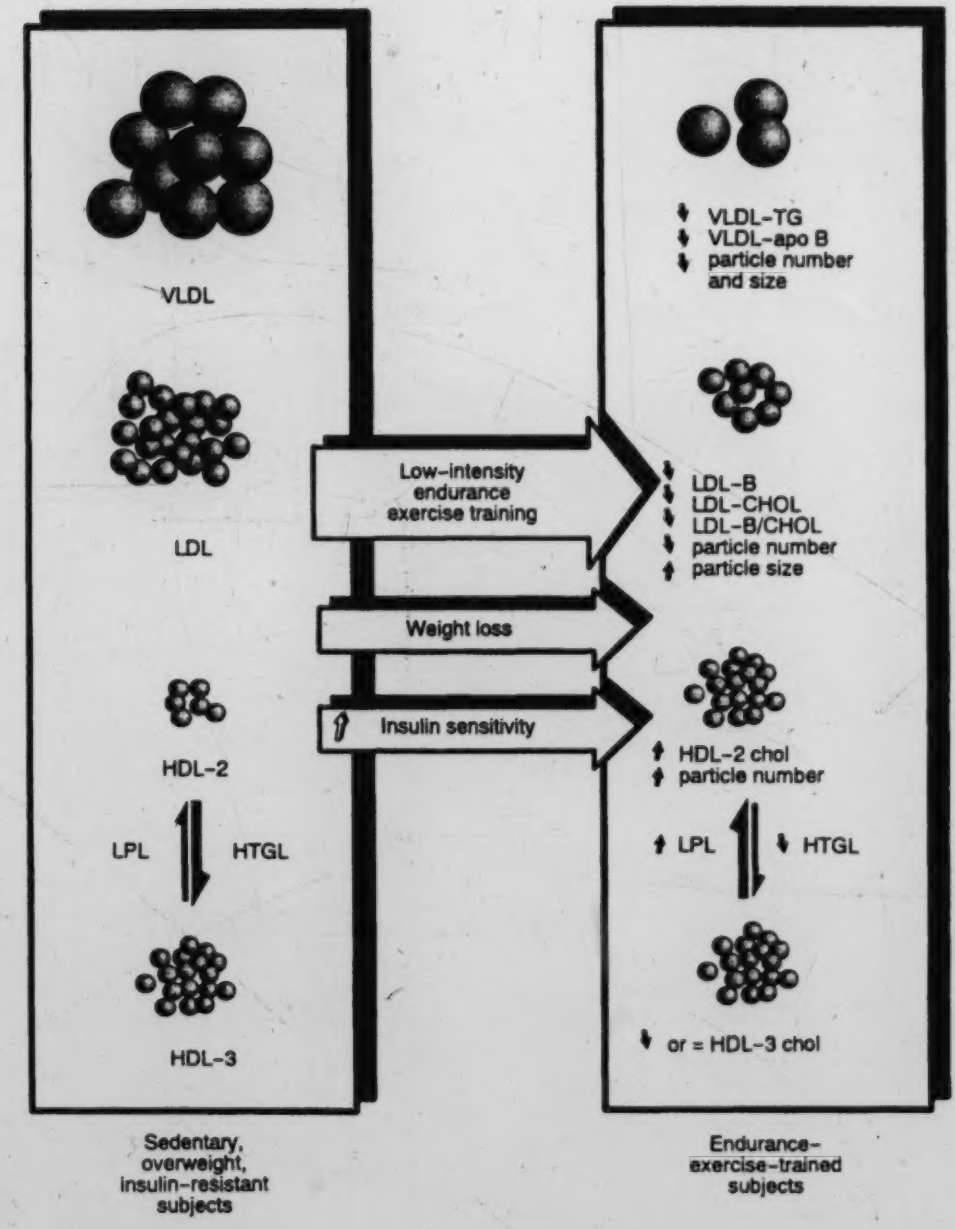
Also, it is possible that weight loss played an important role in the HDL increase, for research shows a correlation between weight loss and increased HDL cholesterol. One study, which investigated the effects of weight loss with caloric restriction versus caloric expenditure in 155 sedentary men aged 30-59 years, 20-60% over Metropolitan ideal weight, found that the difference in HDL_2 was attributed to exercisers' reduced BMI [weight (kg)/ height $(m)^2$] (Williams et al., 1990). Most of the differences in lipoprotein levels between the experimental and control groups were attributed to weight loss (Williams et al., 1990). In support of this conclusion, Van Gaal, Wauters, and De Leeuw (1997) reported that moderate weight loss (5-10%) had beneficial effects on CVD risk factors and that when moderate weight loss was combined with exercise, TG significantly decreased and HDL levels increased. The mechanism by which weight loss increases

HDL levels has been reported to result through decreased HDL binding to adipose tissue (Després et al., 1995).

The fact that serum TG decreased in this study indicated that TG-rich lipoproteins were being catabolized to FFA at adipose and muscle sites by LPL for immediate energy and storage uptake (Tikannen et al., 1996). TG may have also been affected by dietary fat consumption, for fat increases VLDL production, subsequent degradation of VLDL at the muscle and tissue sites, TG uptake, and HDL_2 formation (Fernandez et al., 1995).

LDL and thus TC may have increased due to augmented catabolism of TG-rich lipoproteins which would result in a rise in IDL and LDL levels (Fernandez et al., 1995). LDL may have also been increased as a result of a high fat diet in some subjects for literature in the area of lipid and human nutrition has suggested that saturated fat increases and polyunsaturated fat reduces LDL levels (McPherson & Spiller, 1996). Increased fat would increase hepatic cholesteryl ester and cholesteryl rich VLDL, and by the action of LPL, VLDL could be more readily converted to LDL through the delipidation cascade leading to the down regulation of hepatic apo B/E receptors (Fernandez et al., 1995). Finally, it is also possible that the apparent increase in LDL was masking increased particle size and composition that has been shown to occur with endurance training (Després & Lamarche, 1994)(see Figure 5.1).

Figure 5.1. Summary of the effects of prolonged endurance-exercise training in initially sedentary, overweight individuals. Daily prolonged low-intensity endurance exercise decreases fasting plasma TG levels as a result of reductions in the number and size of VLDL particles which are the main TG carriers in the fasting state. No change or a slight reduction in plasma LDL levels may be observed, but this apparently small reduction may mask more important changes in LDL particle size and composition. Finally two enzymes that are important correlates of plasma HDL levels show reciprocal responses to endurance-exercise training. LPL activity, which is positively correlated with plasma HDL_2 levels, is increased, whereas HL activity, which is negatively correlated with plasma HDL_2 concentration, is reduced after prolonged endurance-exercise training. From "Low-intensity endurance exercise training, plasma lipoproteins and the risk of coronary heart disease," by J.-P. Després and B. Lamarche, 1993, Journal of Internal Medicine, 236, p. 17. Copyright 1994 by Blackwell Scientific Publications Ltd. Reprinted with permission from publishers.


VLDL
LDL
HDL-2
LPL
HTGL
HDL-3
Sedentary, overweight, insulin-resistant subjects
Low-intensity endurance exercise training
Weight loss
Insulin sensitivity
VLDL-TG
VLDL-apo B
particle number and size
LDL-B
LDL-CHOL
LDL-B/CHOL
particle number
particle size
HDL-2 chol
particle number
LPL
HTGL
or = HDL-3 chol
Endurance-exercise-trained subjects

Difference between Quads and Paras

When the group was separated into Paras and Quads some differences (>10%) were found, but only LDL in Paras showed significant changes over time. In fact, Paras increased LDL and TC levels to a greater extent than Quads after all exercise interventions. These results were surprising as aerobic training usually reduces TC and LDL levels (Buemann & Tremblay, 1996). One possible explanation for increased LDL levels was decreased hepatic clearance as a result of obesity (Fernandez et al., 1995; Després et al., 1995). These elevated LDL levels also explain the high accompanying TC levels as LDL particles contain the majority of plasma cholesterol in humans (Nanjee, Koritnik, Thomas, & Miller, 1990).

Observations through figures and percent change revealed that HDL_2 levels were increased in Quads during FES-A and HE-A while HDL_3 levels were increased in Paras after FES-T, ACE-A and HE-A. Therefore, Quads increased their HDL_2/HDL_3 ratio to a greater extent than Paras after FES-T, FES-A and HE-A. Since an increase in blood flow to muscle, as seen with FES-LCE training, can increase HDL_2 and HDL_3 (Ruys et al., 1989), it is possible to speculate that the absence of HDL_2 or HDL_3 increases after ACE-A in Quads may have been a result of poor blood flow.

Also, TG levels were decreased in Paras after FES-T and HE-A and were decreased in Quads after FES-A and ACE-A. TG levels may have been reduced with FES-LCE training as it would result with increased fat oxidation in paralyzed muscles via LPL (Després & Lamarche, 1994; Fernandez et al., 1995). Changes in TG with ACE-A demonstrated with Quads are perhaps related to increased utilization and development of upper body musculature which would offer a new site for free fatty acid uptake.

Single Subject Analysis

One notable observation was that the female subject did not significantly change any of her lipid-lipoprotein variables in relation to baseline. This observation is not uncommon in short term and long term studies. Failure of several longitudinal studies to demonstrate a significant HDL cholesterol increase with endurance exercise has led to speculation that women are less likely than men to increase HDL with short term training

(Wood et al., 1984). It has been proposed that this diminished ability to increase HDL levels with exercise is due to initially high plasma concentration in the sedentary state, which could make change more difficult to achieve, or to interactions with sex hormones (Wood et al., 1984). In fact, estrogen may have several protective effects including lower total and LDL cholesterol and higher HDL and its subfractions types (Paganini, Dworsky & Krauss, 1996). Also, non-lipid protective mechanisms of estrogen include direct inhibition of LDL degradation, oxidation, and smooth muscle cell proliferation, insulin sensitivity, endothelial cell integrity, lower system blood pressure, vasodilation, decreased platelet aggregation, and the list goes on (Nasr & Breckwoldt, 1998). These protective effects are being increasingly appreciated as CVD remains the major cause of mortality among postmenopausal women (ibid.).

In this study HDL and HDL_2 levels were elevated in subjects 1, 3, and 5 by at least 100%. The most notable increases were after HE-A exercise which required subjects to work at 75% exercise intensity. The increase in HDL and HDL_2 levels in subject #1 could have been attributed to diet changes for calories and fat increased without weight gain, and carbohydrates decreased. Yet, the increases in subject #3 were perhaps also attributed to muscle fibre change, increased blood flow, and VLDL degradation, because calories, carbohydrates and percent fat decreased, and weight did not change. Finally, increases in subject #5 could have been attributed to various factors. First of all, this subject increased exercise endurance and training resistance on the FES-LCE which implies muscle hypertrophy and increased MHC Type I and Type IIa fibres occurred. If this is true then it is possible to assume that increased muscle mass may have increased HDL levels through improved glucose tolerance, improved muscle sensitivity to insulin, improved insulin-sensitive glucose transporters (GLUT4), improved LPL function within the paralyzed tissue, and improved TG-rich particle degradation (Buemann & Tremblay, 1996). Moreover, dietary records showed that calories and percent fat increased in concert with a 7% decrease in total body weight. All of these effects could have been responsible for the noted HDL increase (Buemann & Tremblay, 1996). Of note, the poly/saturated ratio did not change in subjects which suggested there was no relative increase in saturated fat. Therefore, increased HDL levels were not attributed to this factor.

Although weight loss did occur, it was noticeable in only two subjects, one of which was female and the other who was a Para (subject #5). Therefore, data suggest HDL increases were not solely due to weight loss, or to any one factor. Thus, one might contemplate that exercise did not directly influence HDL levels at all, but provided the means in order to achieve body changes (increased muscle mass, weight loss) that would allow alterations in HDL levels to occur. Due to the small sample size, the mechanisms for change are purely speculative and remain to be proven in larger SCI populations.

In this study, two subjects had initial LDL levels at CVD risk levels. As saturated fat has been blamed for elevated LDL levels it was not surprising to find these subjects with polyunsaturated/ saturated fat (p/s) ratios below one. In fact, all subjects had p/s ratios below one. However with training, the p/s fat ratio increased relative to baseline in subjects 3,4,6, and 7 yet LDL levels increased in subjects 3, 4 and 6 and did not change in subject #5. Therefore, increased LDL levels after exercise interventions, particularly HE-A, despite increased p/s ratio indicate that changes were probably not attributed to diet. One prevalent characteristic among the subjects in this study was that they were obese. Obesity, which has been reported to increase FFA in the system, may have been the most plausible reason for increased LDL levels. Increased FFA would have increased VLDL particle size which would have increased LPL and thus VLDL degradation to result in higher LDL levels (Tikkanen et al., 1996). As obesity is related to increased VLDL particles, it is possible that there was an abundant LDL delivery to the liver, which ultimately down regulated the hepatic receptors and increased LDL levels in the blood.

Of note is that TG levels were not particularly at risk for CVD in this study. This was interesting as six out of the eight subjects were considered obese (three Class I and three Class II obese)(Janssen et al., 1997). As obesity is strongly and positively correlated with TG concentration and inversely associated with the level of HDL (Gidez & Eder, 1984) it was anticipated that TG levels would have been elevated and HDL levels would have been depressed at baseline in all six individuals. However, levels were elevated in only two subjects, one of which was considered non-obese and the other class I obese. Another surprising observation was that three subjects increased TG levels to CVD risk levels throughout the study during rest or after FES-A. Typically, TG would be stored

into tissues for subsequent use, however TG remained elevated in the blood indicating that tissues may have become resistant to TG once exercise was completed thus leaving them in the blood.

Overall TC levels in this study increased for the majority of subjects. Usually, increases in TC are attributed to increases in saturated fat and increases in LDL (Cominacini et al., 1996). However, it does not appear that the consumption of polyunsaturated relative to saturated fat decreased. On the other hand, four subjects increased percent fat. Therefore, increases in TC may have been caused by an increase in absolute consumption of saturated fat, however this was not evident in all subjects (eg. subject #4). Thus, it is likely that TC levels were mostly attributed to increased LDL levels.

In terms of comparing this study to others, there was but one study that has investigated lipid-lipoprotein variables with FES-LCE. This study investigated the effects of HDL, HDL_2 and HDL_3 after five months of training with FES-LCE (Brenes et al., 1989). Study results showed significant increases in HDL_3, but no other differences were found. Besides this research, no other study was found and there were no studies that investigated the effects of ACE and HE exercise on lipid variables. Therefore, no comparative analyses were performed.

Dietary Analysis

Dietary analyses showed that there was a significant increase in calories, carbohydrates and fat. Although some subjects gained weight, the increase did not attain statistical significance. Therefore, it is probable that the increased calories in carbohydrates and fat were expended during exercise so that there was no weight gain. In fact, some subjects lost weight. For some, the loss in weight was due to calorie restriction while in others it was due to increased energy expenditure without calorie restriction.

Dietary records were chosen for this study as they are the gold standard method of assessment from which others are compared (Thompson & Byers, 1994). Unfortunately, for this group of people, the dietary record was at times ineffective as some subjects would not eat for an entire day, while others would eat in restaurants and had difficulty

estimating the amount of food that was consumed. Perhaps a 4 day or a 7 day dietary record would have been more accurate and effective for the measurement of lipids (Jackson et al., 1986). However, the three day record was administered three times during the study and some were returned only months later. Therefore, a longer time would perhaps not be effective. The weakness with this record was that it required subjects to be motivated so that meals were written down when they were consumed (Thompson & Byers, 1994). As some individuals were unable to write due to their lesions levels, subjects were using the 24 hour recall rather than recording at the time of eating. Therefore, records were relying more on memory which may not have been as effective at recording actual intakes. The one benefit of using the dietary record in this study was that participants did not seem overly concerned about their intakes, therefore it was assumed that the record did not alter the behaviour of the participants and that they recorded their intake accurately.

Subjects in this study did not receive any feedback or nutritional counselling regarding their dietary records. They were instructed to maintain their diet and normal eating habits. Results showed that subjects as a group consumed approximately 16% protein, 51% carbohydrates and 32% fat. These findings are similar to the recommended 15% protein, 55% carbohydrates and 30% fat of total caloric consumption (NCEP, 1994). However, 32% fat which was not significantly different from the recommended 30%, could lead to weight gain and future obesity. Of note, only two subjects ate more than 30% fat in their diet - one of whom ate up to 53% fat- and were coincidently the only two subjects classified as type II obese.

Exercise Testing

Procedures.

In this study the traditional HE test was modified to accommodate the subjects who were not able to increase leg resistance. Therefore, subjects remained at a FES-LCE resistance to complete 30 minutes of leg exercise while the resistance on the arm crank increased in resistance every two minutes.

Heart rate.

Heart rates were significantly higher with ACE than with FES (p=0.012), but not between HE and ACE or FES. Lower heart rate during FES-LCE was also confirmed by Mutton and colleagues (1997). Lower heart rates were due to the low intensity of exercise in FES-LCE, while higher heart rates with ACE were due to poor venous return to the heart causing the heart to beat faster to accommodate increasing work loads. The reason there was no difference between HE and ACE was based on the low heart rates in some subjects while performing HE. A lower heart rate might have been expected due to increased venous return (Figoni et al., 1991;Glaser, 1994) and thus larger stroke volume (Andrews & Wheeler, 1995) with each beat. However, it was believed that there may have also been some interference in electrical signals as subject heart rates were at times as low as 31 beats per minute. This kind of reduced heart rate has also been demonstrated during times of autonomic dysreflexia, but this response was seen only in Paras.

In this study, differences between Quads and Paras were only significant with ACE (p=0.000) where Paras had higher heart rates than Quads. Similar findings were found by Drory, Ohry, Brooks, Dolphin, & Kellermann (1990) who observed that heart rate at peak ACE exercise was markedly lower in subject with cervical lesions than among those with lower lesion levels. The lower heart rates in subjects with cervical lesions were due to the disruption of the sympathetic system due to the spinal injury and due to the reduced availability of muscle mass in the upper extremities (Shephard, Bouhlei, Vanderwalle, & Monod, 1988).

Borg-RPE Scale.

RPE-values during ACE were significantly higher than those in FES-LCE (p=0.000) and recordings were significantly higher with HE than with FES (p=0.000). No significant differences were found between HE and ACE as they were identical in scores (18), suggesting that the maximal intensity of exercise was able to reach upper scores of the scale. On the other hand, scores during maximal FES-LCE testing did not surpass 13, suggesting that rate of perceived exertion did not go beyond 'somewhat hard' during maximal testing.

No significant differences were found when Paras and Quads were compared on RPE-values.

$\underline{VO_2 \text{ max.}}$

Based on the criteria for attaining maximal VO_2, only subjects 4,5,6, and 8 attained maximal VO_2 with ACE testing and subjects 4 and 6 attained maximal testing with HE testing. Reasons for peak values and not maximal values in the other subjects were due to reduced heart rates due to quadriplegia and altered heart rates during HE which was perhaps due to electrical interference. VO_2 values were significantly higher in the HE group (1.42 ± 0.34 L/min; p=0.005) than with FES-LCE (0.80 ± 0.34 L/min), and significantly higher with ACE-A (1.19 ± 0.39 L/min) than with FES-LCE (p=0.002). However there were no differences between Quads and Paras.

Both ACE and HE VO_2 values were higher than reported peak VO_2 values (1.04 L/min) found during wheelchair ergometry exercise (Hooker & Wells, 1989). However, similar findings have been reported by Mutton et al. (1997), Krauss et al. (1993), and Hooker et al. (1992). Mutton et al. (1997) investigated subjects with SCI levels of C5-6 to T12-L1 aged 25-46 years. None of the subjects had been involved in an aerobic training program before the study. Subjects were to perform graded arm, graded leg and graded HE exercise. After HE training, graded HE peak VO_2 and VCO_2 were significantly higher than graded arm and graded leg exercise (Mutton et al., 1997). VO_2 values for graded arm, graded leg, and graded HE were 1.39-1.441 L/min, 1.504-1.567 L/min, and 1.691-1.911 L/min, respectively. These values were higher than those reported by Krauss et al. (1993) which were 0.50-1.00 L/min, 1.10-1.37 L/min and 1.25-1.50 L/min for FES, ACE, and HE, respectively. Hooker et al. (1992) showed that the higher VO_2 attained during HE exercise was nearly additive functions of the values achieved above rest during subpeak ACE ad FES-LCE performed alone. They concluded the data substantiated that the pumping capacity of the heart was able to adequately meet the combined demands of the arms and legs at the power output levels used (Hooker et al., 1992).

The reduced VO_2 values during FES-LCE were probably attributed to 1) the low level of resistance attained during training 2) the reduced muscle mass available for

exercise which was a result of reduced oxidative capacity in skeletal muscle caused by physical inactivity, and 3) the conversion of slow twitch fibers to fast-twitch fibers (Mutton, 1997). Consequently, more fit Quads and Paras, with better voluntary ACE capabilities who can accomplish HE exercise at higher combined absolute power output levels will have a better opportunity to induce central cardiovascular training adaptations than would the less fit (Hooker et al., 1992). Moreover, extremely deconditioned people with SCI who have more to gain from HE exercise training should also incur central cardiovascular training effects (Hooker et a., 1992). Other studies which reported higher levels of VO_2 had a higher overall resistance attained during testing.

Resistance.

The resistance or work rate attained during the FES-LCE testing was 0.94/8 kp (6.1W) with a total power output of 6.22 W. This value was higher than the average (2.3 W) reported by Hooker et al. (1992). The average resistance value reached during ACE testing was 0.86 kg (21.41 W).

Power output.

Power output ranged between 3.92 and 30.21 W which was comparable to the range (0-30W) found by Hooker et al. (1992). The average resistance during the HE testing was 0.75/8 kp on the FES and 0.85 kg (total 25.06 W) on ACE. The average power output was 20.87 W which was similar to average reported power output (21.7 W) in Hooker et al. (1992). In Hooker et al., power output for HE and ACE were similar to those values found by this study (21.7 vs. 19.4 W) and (20.9 vs. 17.4 W) respectively.

Hooker et al. (1992) also found that individual power output ranged between 0-12 W for quadriplegics, which was similar to results in this group which included Quads and Paras. Noteworthy was that this group was previously sedentary with no recent exercise training.

Exercise Training

In many FES studies, training was initiated with a period of knee extension training where the quadriceps muscle was exercised against increased loads (Brenes et al., 1989; Mohr et al., 1997). In this study, it was decided, based on numerous subjects who trained with knee extension at the Rick Hansen Centre without improved FES-LCE ability, that no knee extension training would be implemented.

Time completed.

Six subjects were able to complete 30 minutes of exercise on the FES-LCE whereas two subjects, #3 and #4, never pedalled more than two minutes. This was also found by a study performed by Mohr and colleagues (1997), who found that subjects capable of only a few minutes each time, had very little progression over training bouts. Observations during this study suggested that the subjects who did not increase leg endurance during FES-T were individuals who had lesions for several years, did not reach skeletal maturity before the accident due to a childhood injury, and had reduced spasticity. However within the three observations, decreased spasticity seemed to be the most plausible reason for the inability to perform FES-LCE, since both subjects had reduced spasticity. No research seems to have reported similar observations. Another reason for decreased ability to perform cycling could have been due to the replacement of leg muscles by fat or fibrous tissue. However, this could have been the case in only one of the two subjects with 40 years post-SCI and not the other with three years post-SCI. One last reason may have been due to post-traumatic syringomyelia or syringohydromyelia which has been shown to decrease motor power and increase wasting and weakness in the lower extremities (Güler-Uysal, Orkun, Cila, & Özgirgin, 1996). Notably, these conditions are extremely rare with an incidence rate between 3.20 and 3.43% depending on diagnosis means (Perrouin-Verbe et al., 1998).

Of note, lipid-lipoprotein profile in subjects 3 and 4 changed with FES-LCE and HE-A. Although these changes were much smaller than those seen in subject's 1 and 5, results did not clearly show that increased cycling time would have resulted in larger changes.

Work rate.

The work rate was significantly higher with ACE-A than with FES-A ($p=0.008$) and significantly higher with HE-A than with FES-A ($p=0.001$). However, the resistance attained during exercise training was lower than that attained in other studies of equal duration (Mohr et al., 1997). One study found that at the end of a one year period, one subject cycled most of the time at 0 W, three subjects at 6 W, three at 12 W and three at 18 W (Mohr et al. 1997). In this study, two subjects never attained 30 minutes at 0 W, four cycled most of the time at 6.1 W, and two at 12 W.

In addition, work rate was significantly higher in Paras than Quads for HE-A ($p=0.006$) and with ACE-A ($p=0.004$).

Power output.

Power outputs were significantly higher with ACE-A compared to FES-A ($p=0.016$) and significantly higher with HE-A than with FES-A ($p=0.009$). In fact, subjects in the present study were able to complete only 2.95 W with FES-A. These power outputs were extremely low when compared to those of individuals without SCI who performed voluntary cycling and FES-LCE with epidural anaesthesia on the same equipment (Kjær et al., 1994). Results showed that power output was 80-120 W with voluntary cycling in contrast to 20-40 W with FES-LCE.

On the other hand, a power output of 0 W may not accurately reflect the actual increase in metabolic rate above basal and has to be taken with some caution (Mohr et al., 1997). Due to the initial inertia of the flywheel, the wider seat for additional support, efficiency of electrically induced movements relative to that of voluntary exercise, a power output of near zero should not necessarily be considered useless from a training perspective. Also, it was possible that the severe deconditioning in this subject group required more training than just eight weeks. In addition, this study might have required more familiarization with FES-LCE as many studies recruited subjects who were already familiarized with the FES-LCE or required subjects to be able to complete 30 minutes on the FES-LCE before beginning to count training sessions (Mutton et al., 1997).

Power outputs were significantly higher in Paras than with Quads during ACE-A

(p=0.009) and HE-A (p=0.007). This was not surprising as Paras were able to work at a higher resistance than Quads due to their stronger upper body.

Intensity.

Subjects exercised at approximately 75% of maximum ACE resistance and the highest level of FES-LCE at which that they could complete 30 minutes. Some subjects reduced the resistance on the arm crank, but most kept the resistance the same. Subjects who left the resistance the same on the ACE were Quads. This coincides with Hooker et al. (1992) who showed that combined intensities were complementary for enabling HE exercise to be performed without circulatory limitations in people with quadriplegia. The average work rate was 25.06 W which was in the range of the work rate increase found by Mutton et al. (1997) which was 22.2 to 32.4 W. Reasons subjects may not have achieved levels as high as those in Mutton et al. (1997) was probably as a result of the 24 weeks (42 sessions) of HE exercise used in their study as opposed to the four consecutive day exercise intervention used in the present study.

Caloric expenditure.

The caloric expenditure found by a study performed by Mutton et al. (1997) was 150-200 or 300-400 kcal/week during FES-LCE and 250-300 or 500-600 kcal/week during HE exercise. Although similar, HE-A elicited between 100-200 kcal/session compared to FES-A which elicited between 40-120 kcal/session. ACE-A which was also used in the present study, elicited between 60-180 kcal/session. In this study, results showed that ACE-A was significantly higher than FES-A (p=0.004), HE-A was significantly higher than ACE-A (p=0.002), and that HE-A was significantly higher than ACE-A (p=0.000). Quads and Paras differed only during ACE-A where Paras were significantly higher than Quads (p=0.017). Since these exercises were all performed four times a week, the total energy expenditure was 400-800 kcal/week, 240-480 kcal/week, and 360-720kcal/week for HE-A, FES-A, and ACE-A, respectively. However, if HE-A or FES-A were performed only three times a week, kcal/week would be similar to that reported by Mutton et al. (1997). Notably, FES-A was slightly lower in this study to the

decreased resistance of exercise. Due to the recommended 500-3500 kcal/week for reducing death from CVD (Paffenbarger et al., 1986), HE-A would be the optimal choice for exercise. Both FES-A and ACE-A would be sufficient for people with paraplegia as they represent the higher value in the range. People with quadriplegia who were at the low end of the range would probably benefit to a greater extent with HE-A in terms of energy expenditure.

Correlations

In this study, the female subject had higher HDL levels than the males. This finding was consistent with a cross-sectional study where 307 older individuals (169 men; 138 women) aged 67 ± 7 years, were characterized for HDL, leisure time physical activity, peak VO_2, body composition, body fat distribution, and dietary intake (Fonong, et al., 1996). Results showed that HDL was 19% higher in women (1.46 mmol/L or 57 ± 14 mg/dl) versus men (1.23 mmol/L or 48 ± 14 mg/dl).

In this study, BMI correlated positively to weight (r=0.76) and weight correlated negatively with HDL_2 and HDL_2/HDL_3 ratio. Thus, BMI correlated negatively with HDL_2 and HDL_2/HDL_3 ratio. Similarly, in a study on persons without disabilities, it was found that BMI correlated significantly and negatively with HDL_2 changes (Williams et al., 1990). It was also found that weight loss correlated positively and significantly with minimal LDL changes in exercisers, dieters and controls. However, researchers concluded that LDL measurement might be insensitive to changes in LDL distribution because of its nonspecificity in that it encompasses small LDL, large LDL and IDL (Williams et al., 1990). Moreover, the significant correlations between exercisers' lipoprotein changes, their distance run and their increased fitness, were largely ascribed to weight loss (Williams et al., 1990).

In addition, Janssen and colleagues (1997) examined the relation between lipid-lipoprotein profile, and selected factors. Correlations showed that TC and LDL were significantly and directly related to age, TSI, sum of four skin folds, and body mass. Although, many of these factors were not examined in this study, some of the authors findings were very similar.

The present study showed that HDL_2 was inversely related to BMI and body mass. Similarly Janssen et al. (1997) found that BMI together with alcohol consumption accounted for 26% of the variance in HDL_2. Alcohol consumption accounted for 12 % of variance in HDL and the consumption of one drink per day was associated with HDL 0.035 mmol/L higher. In addition, it has been shown that HDL and HDL_2 were related to percentage fat and diet which both directly affect body mass and BMI. In one case, Fonong et al. (1996) found that 32% of the variation in HDL in older men was explained by waist circumference (r^2 = 16 %), percent dietary intake of alcohol (r^2=11%), and carbohydrate (r^2=6%). Waist circumference was also the best predictor of HDL in older women (r^2=7%) with percent dietary intake of carbohydrate adding 6% to the model. Neither peak VO_2 nor leisure time physical activity were independent predictors of HDL (Fonong et al., 1996). In this study, HDL_3 levels correlated positively with average poly/saturated fat ratio whereas in Janssen et al. these levels were not related to any parameter.

TG levels correlated with HDL and HDL_2 levels (r=-0.75) throughout the study which was similar to the inverse correlation (r=-0.67) found by Janssen et al. Researchers concluded that the tendency toward lower HDL levels could be related to the higher TG (1.6 mmol/L) compared to values (1.1 ±1.4 mmol/L) found in able-bodied. Therefore, LDL/HDL was suggested to be a better CVD risk indicator than TC or HDL in persons with SCI (Janssen et al., 1997). Hours of weekly sport participation accounted for a 4% to 6% variance in TC and LDL. One hour more of sport participation was associated with a 0.05 mmol/L reduction in TC levels and a 0.07 mmol/L reduction in LDL levels.

CHAPTER 6

SUMMARY AND CONCLUSION

Research has shown that moderate intensity exercise increases HDL, HDL_2, and HDL_3 levels, decreases TG, and maintains or decreases LDL and TC levels (Buemann & Tremblay, 1996; Després & Lamarche, 1994). Although this has been proven true in nondisabled people, there has been sparse research investigating the effects of exercise in people with disabilities. Therefore, the purpose of this study was to investigate the effects of acute moderate exercise on the lipid-lipoprotein profile in people with SCI. The SCI population was selected as it is at the low end of the physical activity spectrum and physical inactivity is a major risk factor for CVD (Arrol & Swinburn, 1994).

Four different exercise treatments, FES-T, FES-A, ACE-A, and HE-A, were implemented to determine the effects of moderate intensity exercise on LDL, TG, TC, HDL and HDL_2 and HDL_3 levels and TC/HDL and HDL_2/HDL_3 ratio. For this purpose, eight persons with SCI, four of which were Quads and four of which were Paras, were recruited from the Edmonton population. All participants, except for one, were males.

All subjects performed eight weeks of FES-T which was incorporated into the study as preparatory training for FES-A, ACE-A, and HE-A which included four consecutive days of training at a 75% training intensity. Each treatment was followed with one week of rest. Blood samples were taken before and after each treatment. Other variables such as diet, weight, work rate, power output, energy expenditure were monitored in order to explain the trends in lipid-lipoprotein profile.

Results showed no statistically significant findings in the lipid-lipoprotein profile after all treatments. However, after following each individual through a single subject design, trends became evident. Noteworthy were the increased HDL levels with HE-A training, and increased TC and LDL and decreased TG with all treatments.

Potential mechanisms for the increased HDL levels were 1) increased slow oxidative MHC Type I and Type Ia fibres, increased insulin sensitivity in trained paralyzed muscle, increased dietary fat, and increased LPL activity at muscle and adipose tissues (Andersen et al., 1996; Després & Lamarche, 1994, Felber et al., 1993; Fernandez

et al., 1995). Increased LPL activity would increase TG uptake in muscles which could have accounted for decreased TG levels with exercise in most subjects. Increased dietary fat consumption would have also increased TG uptake in the muscles and contributed to the decreased TG levels (Fernandez et al., 1995). Although these mechanisms are well stated in the literature, those for LDL degradation are less clear. However, LDL levels have been reported to increase with more consumption of saturated fats (Felber et al., 1993; Buemann & Tremblay, 1996; Cominacini, et al., 1996; Myant, 1990). Increased TC levels could also attribute to increased LDL levels as they contain the majority of plasma cholesterol in humans (Nanjee et al., 1990).

Based on these conclusions, exercise at moderate intensity tended to improve lipid-lipoprotein profile but these did not reach statistical significance. Therefore, many of the initial hypotheses based on the purpose of this study were rejected. These hypotheses are included in the following section.

The first hypothesis, which was the primary purpose of this study, was to determine whether four bouts of exercise with FES-A, ACE-A, HE-A at 75% exercise intensity would elicit changes in HDL, HDL_2, HDL_3, LDL, TG, and TC levels. It was hypothesized that exercise with ACE-A and HE-A would improve HDL, HDL_2 and HDL_3 and reduce TG and TC levels. Increases in HDL particles were anticipated with ACE-A and HE-A exercise due to increasing intensity of exercise. A reduction in TG was also expected with HE-A compared to ACE-A due to increased caloric expenditure, intensity and work performed. However, there were no significant findings in lipid-lipoprotein profile. After calculating percent change, insignificant trends showed that HDL, HDL_2, and HDL_2/HDL_3 ratio increased to a greater extent with HE-A training. TG levels decreased with exercise, but TC levels and LDL levels increased with all interventions. Increased TC levels were attributed to increases in both LDL and HDL. Both LDL and HDL increased and there was no change in the HDL/LDL ratio (see Table 4.2). Therefore, as moderate intensity ACE-A and HE-A exercise did not significantly increase any variables in the lipid-lipoprotein profile and , this hypothesis was rejected.

The second hypothesis stated that FES-T and FES-A training would not elicit changes in HDL, HDL_2, or HDL_3, however TG and TC would be reduced. Data showed

that FES-T and FES-T did not alter HDL, HDL_2, HDL_3, and TC levels. TG levels decreased in most of the subjects, but this change did not reach significance. Therefore the second hypothesis was rejected.

The third hypothesis stated that there would be no changes in LDL after performing FES-T, FES-A, ACE-A, or HE-A. Results show that exercise tended to increase LDL levels, but increases did not reach statistical significance. Therefore, this hypothesis was accepted.

The fourth hypothesis stated that were would be no differences in lipid-lipoproteins profile with people with quadriplegia or paraplegia relative to baseline. Results indicated that there were significant changes in LDL levels ($p=0.046$, $p=0.05$) only in Paras. No other significant findings were evident in Paras and in Quads. Therefore, the data resulted in the rejection of the hypothesis and indicated that when Paras and Quads were separated, LDL in Paras were significantly increased over time with exercise training.

The fifth hypothesis stated there would be no differences in the lipid-lipoprotein profile between people with quadriplegia and those with paraplegia at baseline and with exercise. Results demonstrated no statistically significant differences between Quads and Paras before and after training with each exercise intervention which agrees with the hypothesis. However, after calculating percent change, trends were evident. Paras increased HDL levels with ACE-A and HE-A whereas Quads increased with FES-A and HE-A. HDL_2 levels increased with FES-T, ACE-A and HE-A in Paras, but increased to a much larger extent in Quads during FES-A and HE-A. Quads increased HDL_3 in FES-T, ACE-A, and HE-A however no change was found in Paras. Quads increased HDL_2/HDL_3 ratio to a greater extent with FES-T, FES-A, and HE-A, and did not change in Paras. Paras increased LDL levels in FES-A and HE-A, whereas Quads did not change. TG levels decreased with FES-T and HE-A in Paras and Quads decreased with FES-A and ACE-A. Paras increased TC in HE-A , FES-A and ACE-A and no changes occurred for Quads. Although dietary fat and muscle mass may have increased more so in Paras, it was difficult to make any conclusions based on the small sample size.

The sixth hypothesis stated that trends in lipid-lipoprotein profile would be evident in subjects after single subject analyses. This hypothesis was proven true, since subjects 1, 3, and 5 increased HDL's to a greater extent with HE-A than any of the other subjects. These increases in HDL levels in subjects 1 and 5 were attributed to performance increases, while increases in subject 3 may have been attributed to initially low levels of aerobic fitness. Other trends showed decreased TG levels in all subjects, except for subject number 7. LDL and TC levels increased in subjects 3,4,6, 7, and 8, however the increases in subjects 6 were the largest.

The seventh hypothesis stated that weight loss would occur to a greater extent with HE-A than with ACE-A, FES-T, or FES-A. This hypothesis was rejected as only subjects 3 and 5, and 8 lost weight and this weight loss occurred with FES-T exercise.

The eighth hypothesis was that HE-A and ACE-A would elicit superior 1) increases in resistance, 2) power output, and 3) energy expenditure than FES-A. The rational for these increases was that HE-A was a combination of both FES-A and ACE-A. Therefore there would be more resistance, more power output, and greater energy expenditure. The results, which agree with the first and second part of the hypothesis, showed that HE-A and ACE-A increased work rate and power output statistically above FES-A but not above ACE-A. HE-A was not statistically greater than ACE-A as ACE-A accounted for a greater percentage (>80%) of total work rate and power output than FES-A (Hooker et al., 1992). Low work rates and power outputs during FES-A were attributed to weak paralyzed leg muscles. On the other hand, if weak paralyzed muscles had become stronger with training, there may have been significantly increased work rates and power outputs with HE-A compared to ACE-A. In contrast, upper body muscles were not paralyzed and were consequently capable of performing more work in ACE-A and HE-A. Notably, the power output was significantly higher for Paras than Quads in ACE-A and HE-A indicating that upper body muscles were statistically stronger in Paras than Quads.

In terms of energy expenditure, HE-A was significantly higher than ACE-A and FES-A which corresponds with the third part of the hypothesis. In addition ACE-A was significantly higher than FES-A. This is due to the fact that arms were stronger than legs and were able to work at a higher intensity. Therefore the work and the intensity

combined were greatest in HE-A, second greatest in ACE-A and lowest in FES-A. Paras were able to expend significantly more calories during ACE-A than Quads. Increased caloric expenditures among Paras were notably due to increased muscle mass availability due to lower lesion levels and subsequently stronger muscles, higher work rates and higher power outputs with ACE-A. Similarly, Paras expended more calories than Quads with HE-A, yet no significant difference was found.

The ninth hypothesis was that heart rate during maximal testing would be highest with ACE, moderately high with HE and lowest with FES-LCE (Krauss et al., 1993). It was thought that ACE would have a higher heart rate than HE because ACE was to be performed in a vertical position and would have greater pooling in the legs and compromised venous return (Krauss et al., 1993). Consequently, the heart would have to beat faster to supply working muscles with enough blood and oxygen to perform work. In contrast, HE would have a lower heart rate due to increased blood return from the lower extremities and would therefore not have to pump as quickly to accommodate the increasing work load. Results, which agree with the hypothesis statement, indicated that HE was indeed lower than ACE, however no statistical difference was found. On the other hand, ACE and HE were both significantly higher than FES-LCE as FES-LCE was performed at a lower intensity and did not require the heart to pump as fast. Differences in heart rates between Paras and Quads were only found during ACE. Lower heart rates in Quads may have been due to a dysfunctional SNS, a reduced venous return, and an early onset of fatigue.

The tenth hypothesis stated that Borg-RPE scale scores would be similar among HE and ACE but lowest with FES-LCE. Similar RPE-values with HE and ACE would be due to the presence of ACE in both modes of exercise and RPE values would be higher with HE and ACE compared to FES-LCE due to the low intensity of FES-LCE relative to that of HE and ACE. Results showed statistically higher RPE-values with HE and ACE than with FES-LCE and no significant difference between HE and ACE. Therefore, the hypothesis was accepted.

The eleventh hypothesis stated that maximal aerobic power would be highest with HE, moderately high in ACE and lowest with FES-LCE. Although this hypothesis was

proven true in that HE and ACE were both significantly higher than FES, there were was no significant difference when HE was compared to ACE. Lack of significance between HE and ACE was due to the weak paralyzed legs during HE (max 1/8 kp) and also due to subject number 7 who did not reach maximal aerobic power during maximal testing.

The twelfth hypothesis stated that Paras would have higher heart rates, RPE-values and maximal aerobic power measurements than Quads during maximal testing. This hypothesis was based on the assumption that Paras would have more upper body musculature available to perform exercise and would therefore be able to attain higher VO_2 with higher corresponding heart rates. Results showed significantly higher heart rates in Paras than Quads during maximal testing. As RPE-values and VO_2 did not change significantly, this hypothesis was rejected.

Although dietary changes were not expected to occur in this study due to the fact that subjects were requested to keep their dietary intakes constant, diet analyses showed changes in diet. Results showed statistically significant changes in calories and an increase in carbohydrates and fat between the second and third dietary record which corresponded to week 9 and week 17 of the study. Therefore it is evident that changes occurred and research has provided substantial evidence to show these changes would have influenced the lipid-lipoprotein profile. In retrospect, it would have been advantageous to follow intakes on a week to week basis to ensure no changes in diet.

Future Directions

The present study demonstrated the potential for HE exercise to reduce obesity and its associated insulin resistance in people with SCI. This statement is based on the fact that HE increased energy expenditure to a greater extent than ACE or FES-LCE. Unfortunately, results did not clearly demonstrate that HE was able to improve the lipid-lipoprotein profile in all subjects. This lack of improvement with HE may be attributed to a carry over effect between exercise treatments which suggests that the allotted one week rest period may have been insufficient for lipids and lipoproteins to return to baseline. Interestingly, research in the nondisabled population had not surpassed 72 hours post-exercise to measure changes in lipid-lipoprotein profile (Cullinane, Siconolfi, Saritelli, &

Thompson, 1982; Davis, Bartoli, & Durstine, 1992; Kantor, Cullinane, Sady, Herbert, & Thompson, 1987). Therefore, five days of rest (120 hours) in this study was believed to be substantially long enough for levels to return to baseline after exercise. However, based on this study, it is possible to conclude that persons with SCI did respond in the same way as persons without a disability. To avoid a carry over effect in persons with SCI, future studies should aim to assess blood lipid-lipoprotein profile using only one exercise modality at a time or implement longer rest periods.

As greater increases were found with HE-A in some subjects, it is recommended that further research be developed with HE and other exercise modes that utilize the upper and lower body such as FES-assisted rowing (ROWSTIM, University of Alberta). The only disadvantage and deterrent to investigating HE is that there is no manufacturer of HE, so that researchers must adapt the FES-LCE to accommodate the ACE. Despite this inconvenience, HE should be investigated in a longitudinal study in order to determine whether training effects occur. In addition, longitudinal studies would provide the body changes that seem to be a prerequisite to improved lipids.

Weight and diet also appeared to influence lipid levels in this study, however changes did not reach statistical significance. In future studies, diet could be controlled from a laboratory so that carbohydrate, fat and protein percentages of total calories would not change. Due to the fact that it is theoretically unrealistic to insist on keeping body fat and caloric intake constant while studying the effects of increased levels of exercise, caloric intake should increase to compensate for increased energy expenditure and resulting decreases in body fat (Wood et al., 1984).

Conclusion

Literature indicates that active people with or without disabilities have increased HDL levels and decreased risk for cardiovascular disease. At this time, there have been many short-term studies looking at the effects of exercise on HDL levels, yet significant changes have rarely been found. It is believed that there is a critical time or critical volume of exercise needed in order for positive changes to occur (Wood et al., 1984). Unfortunately, studies are not long enough in duration to capture this critical time or

volume. It is hypothesized that four weeks, preferably one year, is needed for long term improvements to occur (Wood et al., 1984).

In addition, perhaps it is not only the length of time and volume that are critical, but also weight loss. It appears that HDL changes are produced, by the large increase in energy expenditure required for regular exercise, the balancing caloric intake and the accompanying leanness (Wood et al., 1984). If body mass loss and HDL cholesterol increases are related only indirectly through exercise, then exercise must coincidently affect total body mass and HDL in a similar manner (Wood et al., 1984).

Although people with SCI have a greater risk of CVD than the nondisabled population, research agrees that it is not so much the lesion level that changes lipid and lipoprotein levels, but more the modifiable risk factors such as activity level, smoking, alcohol consumption, body mass index, and adipose tissue (Janssen et al., 1997; Krauss et al., 1993; Yekutiel et al., 1989). Also, some authors suggest that HDL levels alter with BMR, muscle mass, and body girth measurements. If this is the case, a complete lifestyle change is required for changes in lipid-lipoprotein profile to occur. Physical activity thus becomes a means to change body parameters, metabolism, muscle mass, insulin resistance in order to improve lipid-lipoprotein profile.

In terms of choosing a type of exercise to elicit body changes to prevent future CVD in persons with SCI, it appears that HE offers the benefit of increased intensity, increased blood flow, increased energy expenditure and increased muscle mass in the paralyzed musculature. Although ACE also increases intensity of exercise and energy expenditure, blood flow is compromised and the paralyzed insulin resistant muscles in the legs do not benefit from exercise. In addition, ACE has the potential to damage upper body musculature through overuse. Despite the fact that HE included ACE which could also damage upper body musculature, ACE in this mode of exercise can be performed at a lower exercise intensity (50-60% of max). Therefore, it is recommended that people with SCI, particularly Quads, perform HE to improve health and prevent future complications with diabetes and cardiovascular disease.

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APPENDICES

Appendix A- Adult Treatment Panel II

Appendix B- Study Information for the Participant

Appendix C- Consent Form

Appendix D- Study Overview

Appendix E- Sample of the 3-Day Dietary Intake Record

Appendix F- Borg-RPE Scale

Appendix A

Adult Treatment Panel II

Corresponding Levels of Lipids

Corresponding Levels of Lipids in mg/dl and mmol/L

Cholesterol		Triglyceride	
mg/dl	**mmol/L**	**mg/dl**	**mmol/L**
35	0.9	200	2.3
60	1.6	400	4.5
100	2.6	1000	11.3
130	3.4		
160	4.1		
190	4.9		
200	5.2		
220	5.7		
240	6.2		

Note. From Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: National Cholesterol Education Program, (1994). Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adults Treatment Panel II). Circulation, 89, p. 1363. Copyright 1994 by the American Heart Association, Inc. Reprinted with permission of the author.

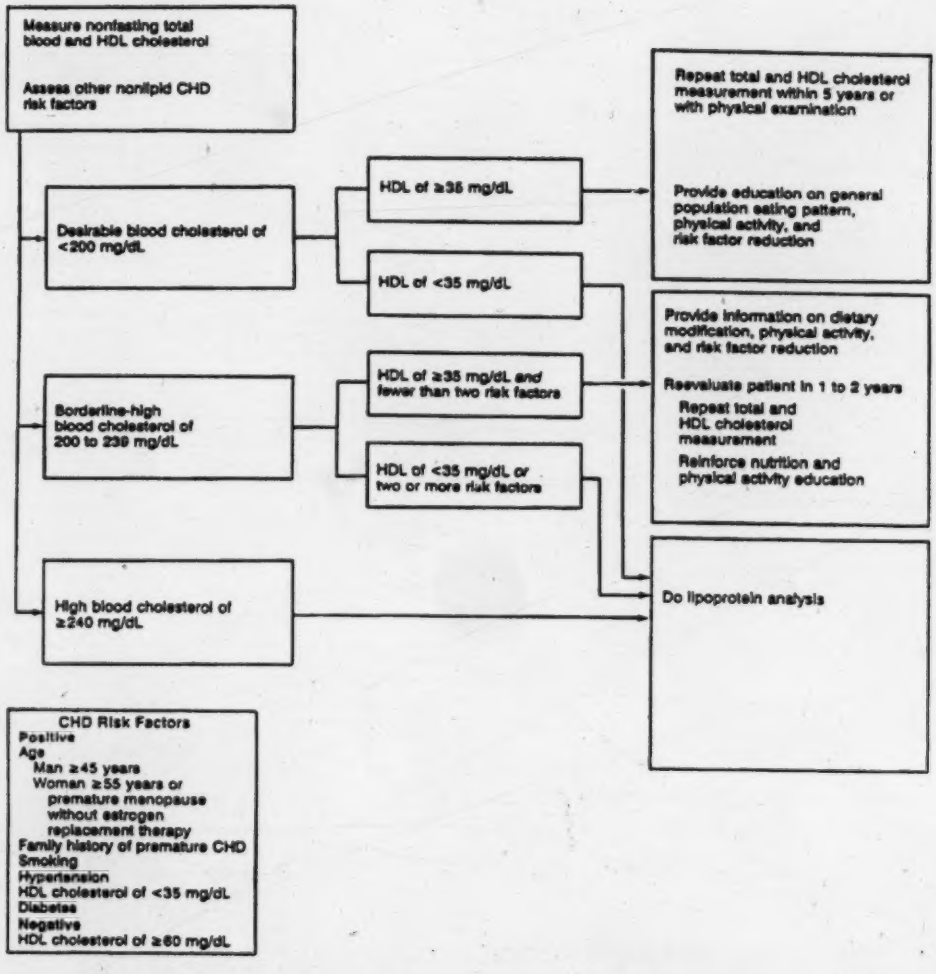

Measure nonfasting total blood and HDL cholesterol
Assess other nonlipid CHD risk factors
Desirable blood cholesterol of <200 mg/dL
Borderline-high blood cholesterol of 200 to 239 mg/dL
High blood cholesterol of ≥240 mg/dL
HDL of ≥35 mg/dL
HDL of <35 mg/dL
HDL of ≥35 mg/dL and fewer than two risk factors
HDL of <35 mg/dL or two or more risk factors
Repeat total and HDL cholesterol measurement within 5 years or with physical examination
Provide education on general population eating pattern, physical activity, and risk factor reduction
Provide information on dietary modification, physical activity, and risk factor reduction
Reevaluate patient in 1 to 2 years
Repeat total and HDL cholesterol measurement
Reinforce nutrition and physical activity education
Do lipoprotein analysis
CHD Risk Factors
Positive
Age
Man ≥45 years
Woman ≥55 years or premature menopause without estrogen replacement therapy
Family history of premature CHD
Smoking
Hypertension
HDL cholesterol of <35 mg/dL
Diabetes
Negative
HDL cholesterol of ≥60 mg/dL

Figure A. Flow chart of primary prevention in adults without evidence of coronary heart disease (CHD). Initial classification is based on total cholesterol and high density lipoprotein (HDL) cholesterol. From Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: National Cholesterol Education Program, (1994). Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). Circulation, 89, p. 1357. Copyright 1994 by the American Heart Association, Inc. Reprinted with permission of the author.

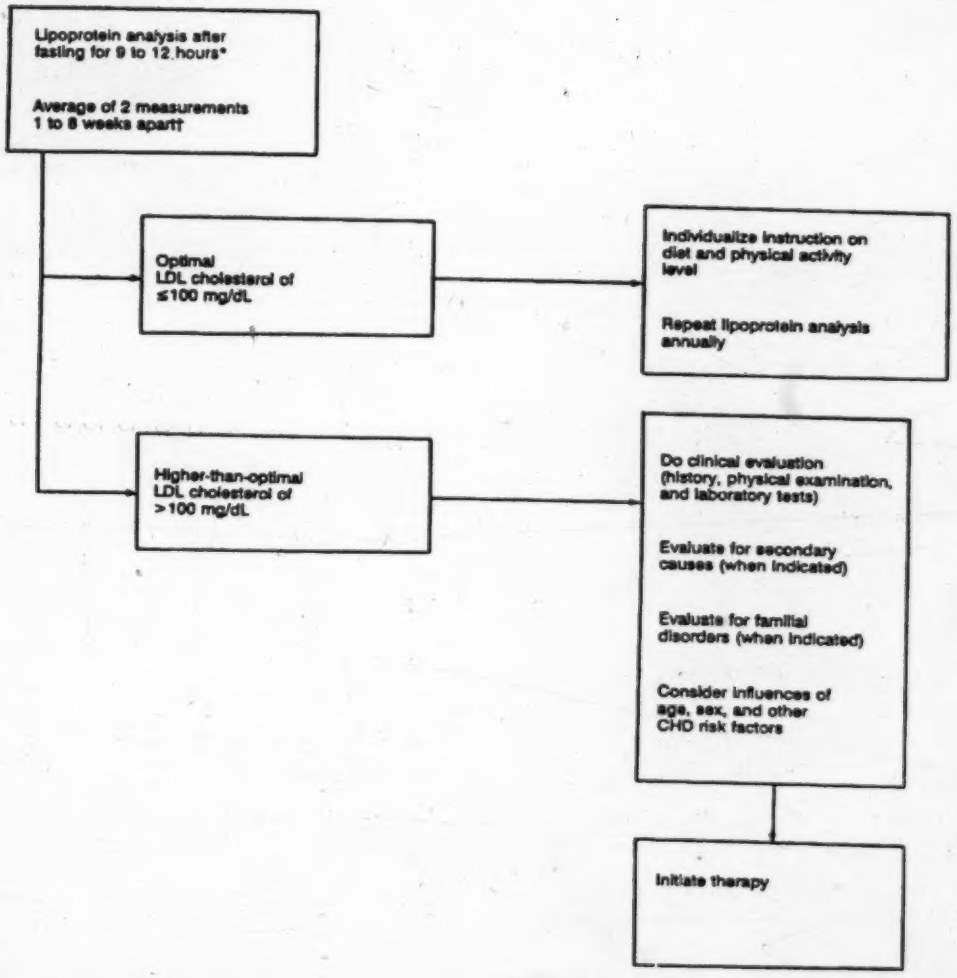

Lipoprotein analysis after fasting for 9 to 12 hours*
Average of 2 measurements 1 to 8 weeks apart†
Optimal LDL cholesterol of ≤100 mg/dL
Individualize instruction on diet and physical activity level
Repeat lipoprotein analysis annually
Higher-than-optimal LDL cholesterol of >100 mg/dL
Do clinical evaluation (history, physical examination, and laboratory tests)
Evaluate for secondary causes (when indicated)
Evaluate for familial disorders (when indicated)
Consider influences of age, sex, and other CHD risk factors
Initiate therapy

Figure B. Flow chart of secondary prevention in adults with evidence of coronary heart disease (CHD). Subsequent classification is based on low density lipoprotein (LDL) cholesterol. *Lipoprotein analysis should be performed when the patient is not in the recovery phase from an acute coronary or other medical event that would lower the usual LDL cholesterol level. †IF the first two LDL cholesterol tests differ by >30 mg/dl, a third test should be obtained within 1 to 8 weeks, and the average value of the three tests should be used. From Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: National Cholesterol Education Program, (1994). Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). Circulation, 89, p. 1359. Copyright 1994 by the American Heart Association, Inc. Reprinted with permission of the author.

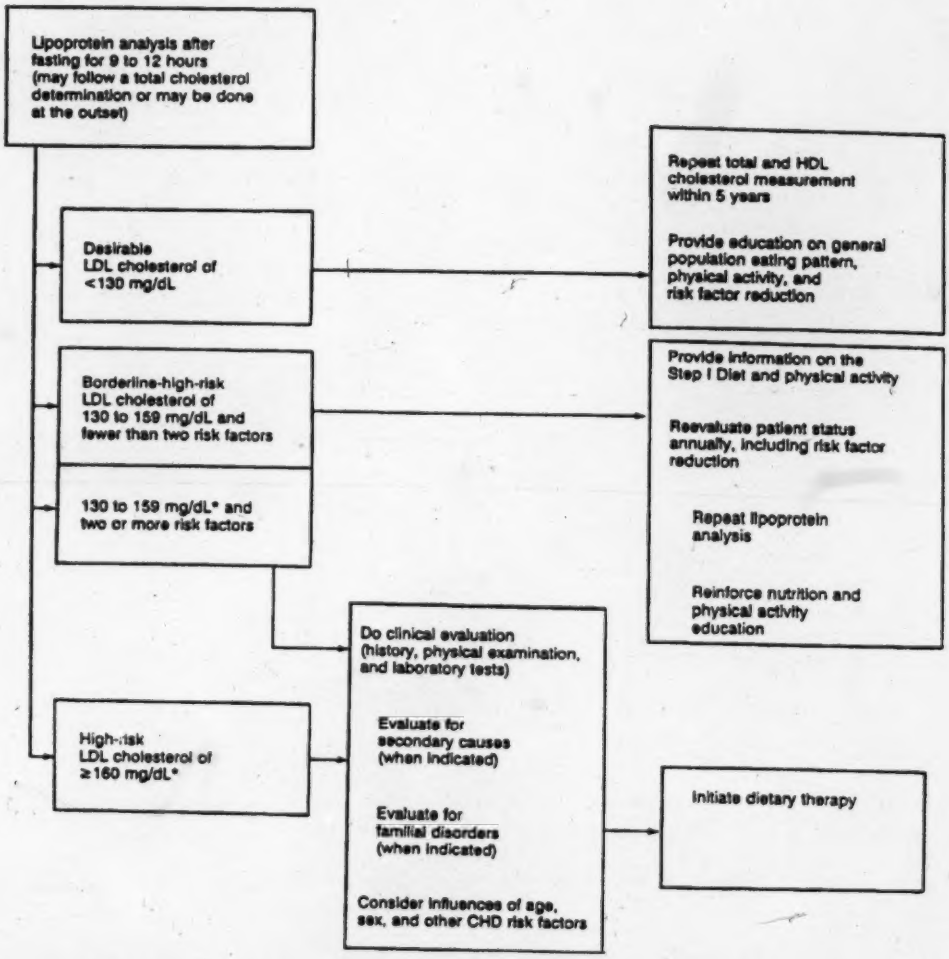

Lipoprotein analysis after fasting for 9 to 12 hours (may follow a total cholesterol determination or may be done at the outset)
Desirable LDL cholesterol of <130 mg/dL
Repeat total and HDL cholesterol measurement within 5 years
Provide education on general population eating pattern, physical activity, and risk factor reduction
Borderline-high-risk LDL cholesterol of 130 to 159 mg/dL and fewer than two risk factors
130 to 159 mg/dL* and two or more risk factors
Provide information on the Step I Diet and physical activity
Reevaluate patient status annually, including risk factor reduction
Repeat lipoprotein analysis
Reinforce nutrition and physical activity education
Do clinical evaluation (history, physical examination, and laboratory tests)
Evaluate for secondary causes (when indicated)
Evaluate for familial disorders (when indicated)
Consider influences of age, sex, and other CHD risk factors
High-risk LDL cholesterol of ≥160 mg/dL*
Initiate dietary therapy

Figure C. Flow chart of primary prevention in adults without evidence of coronary heart disease (CHD). Subsequent classification is based on low density lipoprotein (LDL) cholesterol. * On the basis of the average of two determinations. If the first two LDL cholesterol tests differ by > 30 mg/DL, a third test should be obtained within 1 to 8 weeks, and the average value of three tests should be used. From Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: National Cholesterol Education Program, (1994). Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). Circulation, 89, p. 1358. Copyright 1994 by the American Heart Association, Inc. Reprinted with permission of the author.

Appendix B

Study Information for the Participant

March, 1996

Dear Volunteer,

I am a part of the Rick Hansen Centre staff at the University of Alberta that is conducting a study to determine the effects of exercise on blood parameters known to be associated with cardiovascular disease. It has been shown cardiovascular disease is a leading cause of death, illness and disability in Canada. Reduced levels of high density lipoprotein cholesterol (HDL) and physical inactivity increase the risk of cardiovascular disease in people with spinal cord injury (SCI). Evidence suggests that physical activity has the potential to increase HDL levels in the blood and therefore decrease the risk for cardiovascular disease.

Your participation in this study would help make this the first study identifying changes in risk factors for cardiovascular disease in people with SCI through moderate exercise. This study would require approximately 50 hours of your time over a four month period. During this time, you would have the opportunity to train with functional electrical stimulation, determine your cholesterol levels and temporarily decrease your risk of cardiovascular disease. You would also have the opportunity to become a client of the Rick Hansen Centre. It is hoped that the information gained from this study will increase your understanding of how to prevent cardiovascular disease.

I have attached some further information and an informed consent form. Should you choose to participate in the study, please feel free to contact me at 434-0184.

Sincerely,

Christina Weiss

University of Alberta
Department of Physical Education and Sport Studies

Study Information

Investigators
Dr. R.D. Steadward, Dr. G. A. Francis, Dr. R.S. Burnham, C.B. Weiss

Cardiovascular disease (CVD) is a main cause of death, illness, and disability for people with a spinal cord injury. Since reduced levels of high density lipoprotein cholesterol (HDL-C) and physical inactivity increase the level of risk for CVD to a much greater extent in people with SCI, research on the effects of exercise on HDL-C levels is important. In a study lasting two and a half months, we will isolate the effects of functional electrical stimulation exercise on lipid and lipoprotein levels in the blood, through recording dietary intake and weight before and after the study.

Thirteen subjects will be asked to participate in this study and perform the following procedures:

Functional Electrical Stimulation (FES): FES is an electrical current that is administered to muscles via skin electrodes, to elicit a muscle contraction. Although FES is safe, there are associated risks. One risk is an increase in blood pressure with a decrease in heart rate which occurs as a result of a pain stimulus felt in exercising legs. This can be dangerous, but can be reversed with termination of the stimulus. Another potential risk is tissue damage as a result of the electrodes and electrical current, due to skin sensitivity and impedance to the electrical current. However, the electrodes are coated with gel which helps reduce the impedance of the current to minimize tissue damage.

FES Leg Cycling Ergometry Training: This training will require the subject to perform twenty four 30 minute sessions of leg cycling ergometry in eight weeks. Each 30 minute bout of exercise will require 15 minutes for subject preparation and 15 rest. **Time requirement: 24 hours.**

Acute FES Leg Cycling Ergometry Training: This training will require individuals to perform six 30 minute sessions of leg cycling ergometry in one week. Each 30 minute bout of exercise will require 15 minutes for subject preparation and 15 rest. **Time requirement: 6 hours.**

Arm Crank Ergometry Training: This training will require individuals to perform six 30 minute sessions of arm cycling exercise in one week. Each sessions will require 10 minutes to change and 30 minutes of exercise. **Time requirement: 4 hours.**

Hybrid Training: This will require the subject to perform arm cranking exercise and FES leg cycling ergometry at the same time. There will be six 30 minute sessions of exercise in one week. Each 30 minute bout of exercise will require 15 minutes for subject preparation and 15 rest. **Time requirement: 6 hours.**

Medical Examination: This exam will include: family history, an assessment of cardiovascular disease risk factors, medication, alcohol consumption, tobacco, drug usage, physical exam. The physical exam will include a body assessment of spasticity, pressure sores, lung sounds,

abnormalities, and an FES trial to determine any evidence of a reduced heart rate and increased blood pressure. **Time requirement: ~ 1 hour**

Lipid lipoprotein profile analysis: Subject's will be required to fast for 12 hours prior to blood sample withdrawal, and avoid alcohol consumption. A qualified phlebotomist will perform the venipuncture and collect a total of 20 ml of blood in one setting. There will be 7 settings where blood will be drawn. There is a risk of discomfort/ bruising from venipuncture. These samples will then be taken to the University of Alberta Hospital for analysis. **Time requirement: 5 minutes x 9 = 45 minutes.**

Dietary Intake: will be assessed through a 24-hour recall of food and beverage consumption, and by a self-administered 3-day dietary intake record. The 24-hour recall will require an interviewer to probe information from the participant regarding the preceding day's consumption. This should only take 20 minutes. The 3-day dietary record will be completed by a subject on two week days and one weekend day. Each entry should take 5 minutes after every meal. The subject will be required to complete dietary intakes before and after the study. **Time requirement: ~ 4.5 hours.**

Maximal Arm Crank Ergometry: is a maximal test which requires a subject to exercise on an arm crank ergometer that will be increased in resistance until volitional fatigue. **Time requirement: 30 minutes for preparation of the subject and 12-15 minutes of testing time = ~ 1hour**

Maximal Hybrid Ergometry Exercise: is a maximal test which requires subjects to exercise with both the arm crank ergometer and the functional electrical stimulated leg cycle ergometer (FES-LCE) until volitional fatigue. This test will take approximately 12 minutes to complete. **Time requirement: 30 minutes for preparation of the subject and 12-15 minutes testing time = ~ 1 hour**

YOUR TIME COMMITMENT IN THIS STUDY SHOULD NOT EXCEED: 50 HOURS IN 4 MONTHS.

We encourage any questions of clarification or concern you might have about the study. Please contact Christina Weiss @ 434-0184 or Dr. Robert Steadward @ 492-3182 for any additional information.

Appendix C

Form of Consent

Rick Hansen Centre
University of Alberta
Department of Physical Education and Recreation

Participant Consent

Effects of acute moderate intensity FES-leg cycle, arm crank, and hybrid ergometer exercise on lipid-lipoprotein profile in persons with spinal cord injury

Investigators

Dr. R.D. Steadward, Dr. R.S. Burnham, Dr. G.A. Francis, and C.B. Weiss

I _____ (please print your name here) hereby consent to participate in this study. In doing so, I fully understand all the following statements:

1. The study will collect information on dietary intake, weight, blood parameters, heart rate, blood pressure, maximal oxygen consumption, maximal workloads, and energy expenditure. The study will require a 50 hour commitment in four months.

2. I understand the potential risks (see attached information sheet) and benefits of functional electrical stimulation.

3. I understand I will be performing two maximal tests. One test on an arm crank ergometer and another on the hybrid ergometer (combination of arm crank ergometry and functional electrical stimulated leg cycle ergometer). These tests require maximal exertion and may cause shortness of breath, dizziness and perhaps medical complications. Due to this exertion, there will be a physician present and I may call on him/her at any time for assistance.

4. I understand my right to confidentiality will be fully protected throughout the study, in the future and in any published materials and understand that my name will be coded by an ID number.

5. I understand the study as it has been described and acknowledge that I may withdraw from the study at any time, if I so desire, without any penalty.

6. I hereby make available to Christina Weiss and her committee the results of my performance.

7. The study has been explained to me in full and that all my questions have been answered to my satisfaction.

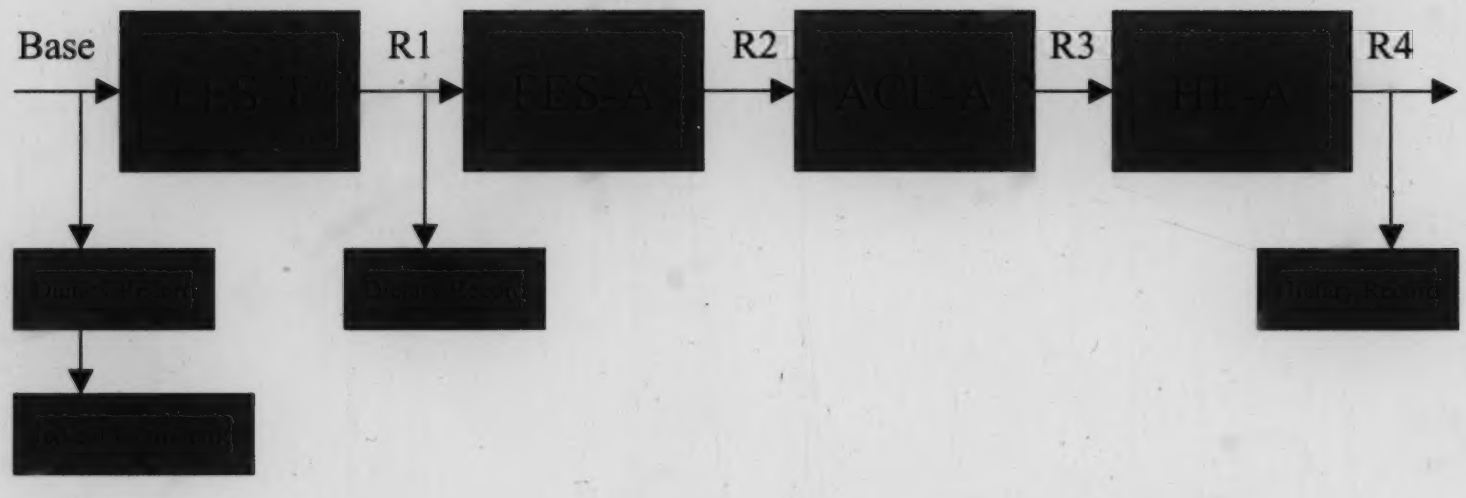
_____	_____	_____
Volunteer name (print)	Volunteer signature	Date
_____	_____	_____
Witness name (print)	Witness signature	Date
_____	_____	_____
Investigator name (print)	Investigator signature	Date

Please contact Christina Weiss (403) 434-0184 or Dr. Robert Steadward (403) 492-3182 if you have any questions about the study

Appendix D

Study Overview

Study Overview



Base: Baseline

FES-T: Functional Electrical Stimulation Training (8 wks)

FES-A: FES Acute training (1 wk)

ACE-A: Arm Crank Ergometer Acute training (1wk)

HE-A: Hybrid Ergometer Acute training (1 wk)

R1,2,3,4: Rest period 1,2,3,4.

Note: Blood tests taken: a) twice at baseline; b) pre- and post- FES-T, FES-A, ACE-A, and HE-A; and c) post R4. Weight was measured at Base, R1, R2, R3, and R4.

Appendix E

3-Day Dietary Intake Record

Directions for Daily Menu

The purpose of this record is to discover everything you consume during a three day period. It is important to record all foods and beverages-from a full course family dinner at home to a quick cup of coffee at work. Before you begin to record in your diary, however, please read the following directions and examine closely the sample day. There is a section for every day:
The day is broken into 6 consumption periods:

Morning Meal
Midmorning Snack
Midday Meal
Afternoon Snack
Evening Meal
Evening Snack

Foods and beverages consumed away from home- at work, at a restaurant, or when visiting friends-are just as important as those eaten at home. Therefore, it is important that your record your entries as soon after eating as possible. The following entries should be included in your recording:

1. **Menu Item Column:** Enter in this column all foods, beverages, etc. consumed during the meal or snack, If your family eats two kinds of cereals or has several different types of sandwiches for example. Please record the correct type.

   Enter in the same block as the menu item all toppings or additives used on the menu item at the time of eating (syrups, gravies, butter, milk, sugar, etc.). Please be specific in your entries -maple syrup, 2% lowfat milk, grape jelly, etc.

2. **Unit of Measure Column:** For every menu item and every topping or additive, enter in this column either the word "number", "cup", "ounce", "teaspoon", or "tablespoon". Not only the menu item, but the topping or additive as well, must have its own unit of measure.

3. **Number of Units Column:** In this area, record the number of units consumed. Include the amount of toppings or additives consumed. An estimate of the unit is satisfactory. Actual measuring is unnecessary unless the exact weight, eg. meat, is known.

4. **Description Column:** For every menu item please include in this column:

   the brand (if known)
   the type and flavour (if applicable) ie. homemade strawberry waffles
   the method of cooking (if applicable) ie. scrambled, baked, fried

   It is not necessary to describe the toppings or additives, only the menu item.

5. **"Where Eaten" Category:** Items consumed away form the home are just as important as those items consumed at home. All consumption should be recorded. It is also important, at the end of each meal, to check where that meal was consumed.

   For example, at the morning meal, one of the categories bellow must be checked:
   Eaten at home
   Eaten away from the home
   Did not eat

6. **Daily Check:** After you have finished your recording for the day, go back over your entries and make sure that for every entry (every menu item, and topping or additive), there is an appropriate unit of measure and the corresponding numbers are given. Also check to see that at the end of each meal, the appropriate category is checked.

   What you eat and drink everyday is important and your entry should be as accurate as possible.

Thank you for your participation and co-operation in this study. Please examine carefully the sample day before beginning.

	MENU ITEM		UNIT OF MEAS.	No. of Units	DESCRIPTION OF MENU ITEM		
	Enter all foods, beverages, etc. consumed as menu items. For every menu item, include any toppings or additives added to the menu item at the time of eating		Enter the Word "cup" "ounce" "number" "teaspoon" "tablespoon"		Brand	Type of Flavour	Method of Cooking
MORNING MEAL	Menu Item	eggs	number	3	Porland		scrambled
	Toppings or Additives	ketchup	tablespoon	2			
	Menu Item	sausage links	number	2	Schneider	sausage	fried
	Toppings or Additives						
	Menu Item	whole milk	cup	1	Silverwood		
	Toppings or Additives	choc mix	tablespoon	2			
	Menu Item	corn flakes	cup	2	Kellogg	cornflakes	
	Toppings or Additives	whole milk	cup	1			
		sugar	tsp.	1			
	Menu Item	banana	no.	1			
	Toppings or Additives						
	Menu Item	multi vitamin	number	1	One-A-Day		
	Toppings or Additives						
	Mark (X) One Category	Eaten at Your Home		X			
		Eaten Away From Your Home					
		Did Not Eat					

Sample Day

Appendix F

Borg- Rate of Perceived Exertion (RPE) Scale

Borg- Rate of Perceived Exertion (RPE) Scale

Description.

The Borg-Rate of Perceived Exertion (RPE) Scale consists of 15 grades from six to twenty, giving "RPE-values" ie. ratings of perceived exertion. The scale is to be shown to a subject when the test procedure (or other kind of work) is explained. When using the Scale, the subject is required to answer verbally by saying a number or has to point with their finger at the suitable scale value. For example, in a test of maximum aerobic power, the subject is shown the scale during the last half minute of each work load and asked to say or point to a number according to how hard the work feels (Borg, 1970).

The RPE-scale is practical for it has been shown to grow fairly linear with work load. Also, the correlation between the ratings and the heart rate is very high. In terms of application, RPE-values give a better estimation of the change in physical stress with age than heart rates. This statement is based on the fact that heart rates at a given load remain constant with age despite declining physical working capacity whereas RPE-values increase with age for the same workload (ibid).

Borg-RPE Scale

6

7 ..... Very Very Light

8

9 ..... Light

10

11 ..... Fairly Light

12

13 ..... Somewhat Hard

14

15 ..... Hard

16

17 ..... Very Hard

18

19 ..... Very Very Hard

20